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The Shattuck Lecture: The Changing Pattern of Neurologic Medicine 839
Derek E. Denny-Brown

Treatment of Thoracic Aortic Aneurysms by the "Pack" Method of Intrasaccular Wiring 847
Robert R. Linton and Irad B. Hardy, Jr.

Myasthenia Gravis: Report of a Case with Exophthalmos without Hyperthyroidism, Relieved by Neostigmine 856
Harvey A. Hatch

Medical Progress: Asthma in Children (Concluded) . . . 858
Francis M. Rackemann and Mary C. Edwards

Massachusetts Medical Society 880

Massachusetts Department of Public Health . 880

Nonclinical Notes 881

Medical Intelligence:

The Routine Guaiac Stool Test 864
C. Lawrence Holt

Doctors Afield: Dr. Archagathos, Refugee Physician and Roman Consul 866
Robert W. Buck

Case Records of the Massachusetts General Hospital 867

Editorials:

The Growth of a Specialty 877

Nursing Reorganizes 878

New England's Health 879

Union of Reporting Secretaries 879

Book Reviews 881

Books Received 881

Notices 882

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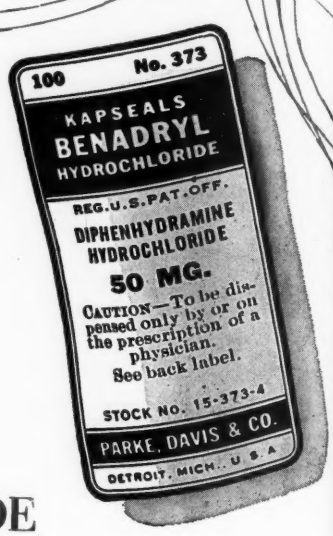

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THE SHATTUCK LECTURE

THE CHANGING PATTERN OF NEUROLOGIC MEDICINE*

DEREK E. DENNY-BROWN, M.D.†

BOSTON

GEORGE CHEYNE SHATTUCK (1784-1854), for whom this lecture was named, adorns that period of medicine that boasts Richard Bright, Thomas Addison, Thomas Hodgkin and Robert Graves. His special attributes were his clinical wisdom, his benevolence and his vision. It was chiefly through him that medicine in New England was set on a firm basis of clinicopathological correlation. The period is notable for the development of the art of clinical observation. In contrast, the first fifty years of the present century will probably be recognized in medical history by the enormous development of methods of measuring pathologic deviations in the living. In our enthusiasm for a scientific approach to problems of disease, the art of medicine has at times been cast overboard and an attempt made to navigate entirely by available laboratory measurement. Such voyages come to grief because no purely laboratory method reveals the whole pattern of the problem. This is particularly true of neurology, in which the pattern of evolution of disease is more important than any one clinical or instrumental finding. Neurology, like any other branch of medicine, must continue to base its methods and philosophy on clinicopathological correlation. Newer scientific technics, however revealing or effective, must in the end be related to the fundamental pathology of the disease process.

The province of neurology in relation to the remainder of modern medicine is so little understood by physicians, — and indeed by many neurologists, — that I must by way of introduction take stock of this situation. It is true that what once was considered by many the unique sphere of the neurologist has changed and is continuing to change, in accord with the rapid developments in medicine in general during the past thirty years. Even in the past ten years, for example, general paresis has practically ceased to appear in general hospitals. In the year 1943 twelve cases were treated in the Neurological Unit of Boston City Hospital. Recently we have treated two cases a year. Tabes dorsalis is also a vanishing disease. Combined-system disease of more than the mildest kind has become a rarity. Those who conceive the function of the neurologist as comprising the diagnosis of cerebral tumor and the diagnosis and treatment of neurosyphilis, multiple sclerosis, epilepsy and a group of rare degenerative diseases of the nervous system may well ask what remains of neurology and what future there may be for young neurologists. Lest it be thought that I am going to bemoan the changing times and the aggressive tendencies of neighboring specialties, let me say immediately that neurology has, on the contrary, entered on an extremely productive and virile phase.

Neurology sprang from internal medicine. Its earlier exponents were internists with a special interest in diseases of the nervous system, many of whom, such as Gowers, Charcot, Strümpell and Pierre Marie, have made notable contributions to subjects other than neurology. In time it was no longer possible to keep abreast of all branches of medicine at once and the genus neurologist was born, joining the dermatologist and later followed by the cardiologist and the gastroenterologist. From the beginning of the budding process the neurologist has occupied a position that is thought to be somewhat academic — the impractical collector of static curiosities and geographer of abstruse anatomic networks, with more than the usual specialist's ritual of cabalistic signs. The rise of neurosurgery as an independent specialty, the success of syphilology in its own field and the mounting aggressiveness of psychiatry soon encroached on what had been considered the neurologist's field, and by the 1930's there were many who predicted the extinction of the genus neurologist. Some professed neurology as an appendage to neurosurgery or psychiatry — and indeed a few professed all three. Many neurologists and neurologic depart-

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ments became absorbed by departments of neurosurgery or else adopted protective coloring in the form of the title "neuropsychiatrist" and still exist in unhappy dependence on these borderlands, fearful lest their patrimony be alienated. The stock in trade, apart from neurosurgical or psychiatric diagnosis, became constricted to the "degenerative" diseases, multiple sclerosis and epilepsy, relieved only by intensive pursuit of electroencephalography and the testing of new drugs on an empiric basis. In relation to places where these circumstances had been reached, it is not surprising that recruits to the banner of neurology should be few. Any physician worth his salt would want to be the neurosurgeon or the psychiatrist and would not remain content to be the poor relation, the dependent diagnostician.

Such an attitude springs from a wrong conception of neurology and an erroneous conception of the structure of medicine. Neurology, to mean anything at all, must mean neurologic medicine and as such must comprise all diseases that in any way affect the nervous system. Since many more diseases may affect the nervous system secondarily than those that attack it exclusively and since more and more of the latter can be shown to be special aspects of the former, neurologic medicine is quite inseparable from internal medicine. The neurologist must be first an internist. His inspiration is in the general medical wards; his technics are those of internal medicine. If neurology ever deserts these, it is doomed to the atrophy that follows inbreeding.

Such atrophy of neurology indeed occurred in many places in the last twenty years. At the Boston City Hospital a planned development of the relation between neurology and internal medicine, in which I have been encouraged by the faith and success of a series of able lieutenants, has had the most happy results. Not only were we especially fortunate in having excellent medical teaching services whose heads welcomed and encouraged our interest in general medical problems, but the directors of the Mallory Institute have encouraged and participated in the development of neuropathology with its special technics of clinicopathological correlation. With such encouragement the cry "back to the medical wards and the autopsy room" has paid handsome dividends. The reason is simply that medicine is the natural field for neurologic medicine and the medical ward and autopsy room comprise the region in which its investigative talents are most usefully employed.

In the past fifty years medical education has undergone great transformation. To the average physician tabes dorsalis is no longer the mystery it was in 1900, and lumbar puncture and its routine interpretation no longer require a consultant. Even disorders like subarachnoid hemorrhage, a neurologic entity twenty-five years ago, are now well understood by most physicians. The neurologist who thinks that he has sole title to the diagnosis and treatment of such diseases or of poliomyelitis or nerve injury is unaware of the changing pattern of medicine. A specialist is only a specialist by virtue of special ability to contribute. If his contribution in one disease has become no longer special, he has presumably applied his talents to some new problems in the meantime. It is not the diseases that are specialized but the talents of the specialist physician, which must be continuously employed in developing new fields to prove their worth.

One further important misconception is that by which a specialist is categorized according to his mastery of an instrument, so that the bronchoscopist, for example, was at first somewhat unwillingly given a right to a view of pulmonary disease but was grudged the right to his own philosophy concerning it. This belittles wisdom and experience and sets a premium on technical ability. A glance at the scale of fees set by national medical-insurance schemes at once shows how poorly expert opinion and advice are rated, compared with the simplest of diagnostic procedures. If this is to be the future pattern of medicine, we may well despair of correcting the deplorable tendency to advise only the trial of this or that wonder-drug, regardless of possible liver damage, agranulocytosis or other risk, heedless of unnecessary expenditure and in ignorance of the natural course of the disease.

These questions are the essence of recurrent misunderstanding concerning specialization in general and neurology in particular. It is the cause of difficulty in the medical-school curriculum, the hospital and the mind of the lay public. If it be acknowledged that every surgeon and every internist has some special field of interest, then each is in some degree a specialist. These questions, therefore, are pertinent to the whole future organization of medicine and should interest every physician. The right to special facilities has to be earned by progressive contribution to the effectiveness of medical practice. Conversely, where neurology has been set up with special facilities in splendid isolation it has tended to wither. For progress it requires its own hospital beds and its own budget; for inspiration it must work with internal medicine.

We might, then, acknowledge that the problems we face in any one branch of medicine are greater than any one of us. The specialist must be prepared both to give and to receive contributions across the arbitrary partitions that separate the various branches. By way of illustrating what I mean in regard to neurologic medicine, we might turn to some special examples.

Liver and Brain

As an example of the kind of problem to which an active department of neurologic medicine can contribute, the relation between liver and brain might first be mentioned, for that has interested us for a number of years. The classic disease process in-

volving these two is Wilson's disease, named for S. A. Kinnier Wilson,[1] who in one stroke demonstrated both the relation between extrapyramidal symptoms and disease of the basal ganglia and established the association of progressive lenticular degeneration with cirrhosis of the liver. Later, forms of the disease without such cavitation ("pseudosclerosis") and the pathognomonic feature of pigmentation of the cornea (the "Kayser–Fleischer ring") were added to the syndrome.[2] These different aspects were shown to be related to different rates of evolution of the disease. It has been found also that these patients show a variable degree of aminoaciduria,[3] a huge deposition of copper pigment in the liver and brain[4] and a consistently high urinary output of copper.[5, 6] The relation between the aminoaciduria and the abnormal copper metabolism is still obscure, although it is clear that the aminoaciduria is not changed by mobilization of some of the excess deposits of the metal in the body through giving the substance 2, 4-dimercaptopropanol (BAL).[5] Yet patient persistence in treatment with this substance results in disappearance of a great part of the patient's neurologic symptomatology[7] in those forms of the disease in which the slow progress and variable signs indicate that actual cavitation has not yet occurred. There now appears no doubt that the neurologic lesions and the pigmentation are due to accumulation of metallic copper in the tissues. It might also be thought that the cirrhosis was interfering with the normal route of excretion of copper via the bile. This is not so, as the biliary output of copper was found to be within normal limits in three cases of the disease.[7]

The problem, therefore, is the nature of the hepatic cirrhosis. It is a coarsely nodular cirrhosis with evidence of recurrent episodes of toxic hepatitis, sometimes obvious in the history, often without history. Portal obstruction is early in some cases and completely absent in others. There is no evidence of inflammatory disease. So far we have no direct clue to the mechanism of the disease, although some collateral facts are extremely suggestive. For example, the accumulation of copper in the tissues and its normal rate of excretion by the normal route are closely paralleled by hemochromatosis, and indeed both hepatolenticular degeneration and hemochromatosis may occur in the same patient.[8] Although hemochromatosis has no specific associated neurologic disorder, prolonged states of drowsiness and torpor are characteristic and are independent of the associated diabetes.[9] Hemochromatosis is also a familial disorder. In addition, there is the rare but well documented occurrence of manganese intoxication, in which hepatic cirrhosis, dysarthria and tremor of the hands result.[10-12] The excellent studies of Hurst[13] showed that manganese can cause cirrhosis, and its occurrence in previously normal persons exposed to manganese salts clearly indicates that here the metal is the primary factor in causation of both the cirrhosis and the neurologic symptoms. The studies of Mallory and Parker demonstrated that copper can likewise lead to cirrhosis. It becomes apparent, therefore, that disordered metabolism of some heavy metallic ions can be of importance in relation to related hepatic and cerebral diseases. The similarity of these disorders suggests that the action of copper is not through a disorder of enzymes of which copper is normally a part but a displacement of some other physiologically important ion by copper.

Apart from the formation of cavities in the basal ganglia, dentate nuclei and frontal lobes in terminal stages of rapidly progressive forms of Wilson's disease, the brain shows only pigmentation in these regions and a diffuse alteration of the glia. The changes in glia cells consist of various degrees of enlargement and proliferation of the astrocytes; this may be the only change in early cases. The similar enlargement of astrocytes found in cases of chronic biliary obstruction by Pollak[14] and in cases of Laennec's cirrhosis with "senile" chorea by Schaltenbrand[15] suggested that the pathogenesis of nervous symptoms in Wilson's disease is not specific for that disease. Adams and Foley[16] have studied the development of hepatic coma at the Boston City Hospital and find that this is indeed true. A fluttering tremor of the wrists when the arms were outstretched was found in cases of hepatic coma, especially recurrent coma. The tremor may appear and disappear in each of several episodes of coma. Foley has observed its persistence for as long as one year after recovery from such episodes in three cases. Adams and Foley[17] have consistently found activation of large astrocytes, comparable to the minimal lesion of Wilson's disease, in the brains of patients who have succumbed to hepatic coma. These observations point to the existence of a single vulnerable metabolic link in hepatic metabolism that can be disturbed in a variety of ways, of which the inborn error of copper metabolism in Wilson's disease is only one. A primary metabolic disturbance of cerebral glia becomes established, parallel to the primary metabolic disorders of cerebral vascular endothelium (Wernicke's encephalopathy, acute hemorrhagic "encephalitis").

Aside from pointing the way in regard to certain aspects of liver disease, such studies open an extraordinary vista of possibilities in neurology. We are fairly certain that disorder of metallic metabolism is not related to diseases such as Parkinsonism, Huntington's chorea, presenile psychoses and familial ataxias, yet it is equally certain that some cumulative metabolic process underlies such "degenerative" diseases. In each of such diseases a progressive cell change documents the gradual failure of specific metabolic processes without gross anatomic lesions. The conception of abiotrophy, or premature senility of cells, now has no real foundation. The

slight degree of anatomic damage in relation to symptoms lends high hope of eventual reversibility when the chemical clues are found.

Our recent experience with young persons presenting the first signs of Wilson's disease has strongly impressed us with the importance of small lapses and irregularities in movement, of the type characteristic of Sydenham's chorea, as an early symptom. This particular symptom has cleared so rapidly with BAL treatment in three cases that I am now sure that it belongs to the disease. We are therefore certain that Sydenham's chorea must itself be a toxic symptom, and we have a new stimulus for seeking its metabolic mechanism.

In Wilson's disease the technics of internal medicine have become applied to a neurologic problem. Although the Kayser-Fleischer ring indicates the presence of Wilson's disease, the definition of the neurologic problem and its extent in any given case requires neurologic experience, especially since the ring is not present in some cases.

Cerebrovascular Disease

Five years ago it might have been thought that there was little more to be said on the subject of cerebral thrombosis and hemiplegia. The description by Moniz and his associates[18] in 1937 of the recurrent cerebral attacks consequent to carotid occlusion did not gain recognition until carotid arteriography came into general use. It then became clear that patients with a history of repeated episodes of weakness of the same limb, usually the upper limb, with or without aphasia, were suffering from the effects of an occlusion of the opposite carotid artery.[19, 20] Over 50 cases have now been described.[21-23] This intriguing syndrome, often attributed to "vasospasm" in the past, is the result of insufficiency of the circulation in the circle of Willis and is usually provoked by circumstances that lower the level of systemic blood pressure, leading to periodic ischemia in the territory now least well supplied by the collateral communicating arteries.[23] Any severe fall in systolic pressure, such as that associated with syncope or intestinal hemorrhage, is likely to provoke a catastrophic necrosis of a large part of the area supplied by the middle cerebral artery.

There are several variants of the syndrome, including attacks of weakness of the lower limb (presumed due to ineffectiveness of an anterior communicating artery) and attacks of blindness in the eye on the side of the carotid occlusion (ineffective collateral circulation of the ophthalmic artery). In time some patients develop a collateral circulation through the external carotid system, via branches of the ciliary and meningeal arteries.[23, 24] The circulation of the ophthalmic artery is then reversed and the internal carotid can be filled from the external carotid. This is an explanation of the later disappearance of attacks of blindness mentioned by Fisher.[22] The cause of the occlusion of the internal carotid is usually atheromatous deposit and arteriosclerotic thickening. It may reach a critical stage in young persons (we have studied a typical patient aged twenty-six). It is frequently associated with arteriosclerotic occlusion of the vessels of the lower limbs. A common history is that of a man of fifty to sixty years of age with a fifteen-year history of peripheral arterial disease who had an unexplained incident of transient paralysis of the right arm with aphasia ten years earlier and who has now commenced to waken from sleep with transient attacks of weakness of the right limbs and difficulty in speech. It is important to realize that the use of vasodilators in such patients may induce a severe hemiparesis. This is a situation in which any dilation of cerebral blood vessels produced by stellate block might be expected to assist the collateral circulation, but in our experience the reverse has been the case.[23] The arguments for and against the usefulness of stellate block have been confused by evidence from cases of sudden hemiplegic catastrophe resulting from ligation of the carotid artery in a young person. This situation is complicated by the effects of sudden reversals of flow in cerebral arteries that may tend to induce spasm by mechanical distention. The result of sudden carotid thrombosis in an elderly atherosclerotic person is usually a fatal coma, possibly due to complete absence of adjustment. The syndrome of obliterating atheromatous carotid occlusion achieves a state of unstable equilibrium through its slowness of onset, but the collateral circulation does not then appear to be regulated by the autonomic nervous system. Cases are on record of bilateral carotid occlusion[25] from this cause with a remarkable intermittent cerebral "claudication" with long periods of survival.

The proof of carotid occlusion in these studies has usually been obtained by arteriography and sometimes by direct surgical exploration of the internal carotid; we are indebted to Dr. Wagner for his co-operation in such procedures in our cases. We would urge caution in the use of arteriography for this purpose in elderly patients, however, for thrombosis can easily be produced in extremely atheromatous vessels. In case of doubt we have found two clinical tests useful: observing the fundus on the side of the suspected lesion and compressing the opposite carotid artery or exerting light pressure on the globe of the eye with the finger. If the retinal vessels derive their circulation from the opposite carotid, they become narrowed by these procedures. These tests are positive in only about half the cases, probably because of the presence of external carotid collaterals in the others. Compression of the carotid on the side of the symptoms will reproduce the symptoms within thirty seconds in about half the cases. The history of repeated episodes of paralysis

in the same limb remains the most characteristic feature of the syndrome.

In carotid insufficiency the most physiologic treatment is one that maintains or raises the level of blood pressure yet obtains some measure of cerebral vasodilation. We have found alcohol by mouth a useful medicine for this purpose and inhalation of air containing 6 per cent carbon dioxide the most effective immediate procedure.

The circle of Willis is also supplied by the basilar artery. This important vessel, in addition to supplying branches to the brain stem, gives rise to the posterior cerebral arteries. Kubik and Adams[26] provided a classical description of the effect of thrombosis of the basilar artery and its occlusion by embolism. The syndrome is very distinctive and is, in fact, common as a terminal event in many atherosclerotic patients. It results in an immediate loss of consciousness, preceded or followed by blindness, and associated with persistent dysarthria with variable degrees of paraplegia or quadriplegia. Commonly the disorder begins in two or three stages, in which an attack of brief loss of consciousness and blindness is followed by signs of bulbar damage and then by stupor with hemiplegia or total paralysis. It is not amenable to more than supportive treatment and is usually fatal after a few days.

The basilar artery is also liable to slow occlusion by atherosclerosis in its lower third,[23] and the resulting insufficiency of the circle of Willis is then comparable to that of carotid occlusion, except that attacks of mental confusion, blindness or unconsciousness, with residual bulbar dysarthria, are the symptoms. As with carotid occlusion, the symptoms are provoked by fall of systemic blood pressure, and stimulation of the circulation provides effective treatment.

Yet another basilar syndrome can be recognized in life, namely, basilar aneurysm. This is a tortuous atherosclerotic fusiform aneurysm and is the result of hypertension in atherosclerotic subjects. The vessel becomes greatly distorted and proceeds to stretch various cranial nerves, particularly the 7th and 8th, sometimes the 5th and 6th, as well as to have its small bulbar side branches occluded one by one.[27] A characteristic attack takes the form of a sudden appearance of intense dizziness with paralysis of the face on one side and loss of hearing, followed by facial spasm and dysarthria, with or without brain-stem damage. At a later date another cranial nerve is suddenly involved in the same way — often the 7th on the opposite side. We have seen deafness become bilateral in three such cases. We have observed 6 patients who, all but one, ultimately made a satisfactory adjustment after being tided over by supportive therapy. Ligation of one vertebral artery has been recommended but appears to us to be somewhat heroic.

It is evident that the most effective management of all these cerebrovascular accidents depends on accurate appreciation of the situation and its effect on cerebral hemodynamics. The principles are relatively simple, and they indicate that good clinical observation and history-taking can obviate the errors that arise from the blind and wholesale application of peripheral vasodilators and stellate block to all "strokes" and may enable avoidance of the risk of arteriography.

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Increased Intracranial Pressure and Pseudotumor

The generalization that brain tumors cause symptoms through increase of intracranial pressure was so thoroughly taught to previous generations of medical students that the notion that increase of intracranial pressure is not the usual cause of symptoms in brain tumor is difficult to explain to an older generation. It is necessary to hold in mind two entirely different mechanisms, the one a distortion of anatomic relations within the skull and the other a rise of intracranial pressure. Each may lead to the other, but the possibility of their independent existence is not generally realized. Investigations of the pathogenesis of headache disclosed that the pressure of the cerebrospinal fluid may be artificially raised to over 500 mm. of water by injection of fluid into the lumbar sac, without causing headache or other discomfort.[28, 29] *Continued high pressure* results in papilledema and retinal hemorrhages from compression of the veins from the retina when they emerge in the sheaths of the optic nerve. If this is continued, it results in optic atrophy and loss of vision. The presence of an *expanding lesion* in the cranial cavity leads to herniation of the midbrain and temporal lobe through the opening in the tentorium and herniation of the tonsils of the cerebellum into the foramen magnum. Herniation of the first type leads to dilated pupil, stupor and a decerebrate state. Herniation at the foramen magnum leads to periodic headache, vomiting, slowing of pulse, drowsiness and eventual respiratory failure. With herniation of either type, circulation of cerebrospinal fluid is ultimately obstructed and pressure inside the cranial cavity is secondarily increased. Raised pressure is then dangerous because it increases the herniation; if prolonged it also leads to papilledema and optic atrophy.

Cerebral tumor may therefore become manifest through its local destructive effects or through displacement of brain substance. Slowly growing benign tumors may cause gross distortion of structure, without actual increase of lumbar or ventricular pressure. Tumors of the brain stem or capsular region lead to little general displacement and therefore give rise to distortion and pressure symptoms only very late in their course. Tumors or cysts in the third or fourth ventricle are the most difficult to diagnose because apart from increased intracranial pressure their local signs are not clear cut,

being early drowsiness and stupor in the former and early vomiting and nystagmus in the latter.

These considerations are important in another respect, for increased intracranial pressure without localizing or distortion signs is the outcome of a series of ill-defined neurologic conditions that are not uncommon. The first and most dramatic of these is meningism, or "serous meningitis," as it was termed by Quincke. This is the transient but sometimes severe increase of intracranial pressure that is associated with the onset of a febrile illness, commonly a pneumonia or otitis media or specific fever. Blurred optic disks, stiff neck and headache are then associated with high lumbar-puncture pressure, but the spinal fluid is unchanged in its contents. The condition is due to acute swelling of the brain, and if spinal fluid is removed too suddenly herniation at the foramen magnum can then occur and be fatal. The condition is related to the sudden drop in electrolytes in the blood serum at the onset of an acute infection.[30, 31] We have demonstrated swelling of the brain and herniation at the foramen magnum in two fatal cases and regard meningism as the result of an osmotic edema of the brain. Although signs of distortion are usually slight, the autopsy findings do not support the earlier hypothesis[31] of increase in formation of cerebrospinal fluid. The condition rights itself in a few hours or days, but if it becomes critical it may be terminated by intravenously given hypertonic solution. It should be emphasized that removal of more than a small amount of spinal fluid is dangerous.

A persistent increase of intracranial pressure, often sufficient to cause prolonged low-grade blurring of the optic disks, is associated with hypertensive heart failure associated with high venous pressure. The defect is then related to defective absorption of cerebrospinal fluid and can be treated by lumbar puncture if headache or papilledema make this necessary. A less well known but more serious disorder of the same kind is "otitic hydrocephalus,"[32] a persistent increased intracranial pressure of severe degree associated with otitis media, less commonly with peritonsillar abscess.[33] In this condition, as Symonds[32] has shown, there is an obstruction of the venous drainage of the sagittal sinus by mural thrombosis, often retrograde from primary thrombosis of lateral sinus. It used to be known as "pseudotumor" or "pseudoabscess," for the severe papilledema leading to optic atrophy has in the past led to fruitless surgical explorations. There are no localizing signs of cerebral damage; headache is mild or absent. The important signs are negative, with one exception. The cerebrospinal fluid is normal in every respect except its increased pressure, and cautious removal, 1 cc. at a time, reveals that the pressure falls only very slowly even though large amounts may be ultimately withdrawn. This last finding indicates that the large amount of fluid itself is the cause of the increased pressure. The appropriate treatment is then repeated lumbar puncture, controlled by pressure readings, to bring the pressure to just below 200 mm. each day, until recanalization of the venous system corrects the defective absorption. Increase of cell or protein content should warn that the infection has penetrated the vein, with likelihood of abscess formation.

We have recently realized that yet another medical condition leading to increased intracranial pressure should be added to this list. Every neurologist has encountered occasional cases of peripheral neuritis with papilledema.[34-39] The occurrence of papilledema in poliomyelitis has also been reported.[40] In a recent case of this kind, that of a thirty-five-year-old man suffering from an infective polyneuritis of considerable severity, we found that the optic disks were becoming swollen in the seventh week of the disease and in the eighth week many flame-shaped hemorrhages had occurred in each retina. The cerebrospinal fluid at this time exhibited a pressure of 390 mm. of water, with no cells, but a protein of 286 mg. per 100 cc. A ventriculogram showed no shift or deformity of the cerebral ventricles. It was only when it was noticed that the spinal fluid clotted spontaneously in the test tube one day in this period that the thought occurred that perhaps clotting *in vivo* was obstructing the Pacchionian villi. Routine daily lumbar puncture was therefore instituted. The pressure fell from 350 to 150 mm. after removal of 10 cc. of fluid. In later daily punctures the pressure fell from 230 to 130-150 mm. after 8 to 10 cc. had been removed. The patient ceased to complain of headache. The papilledema steadily subsided, and no further hemorrhages occurred. After a critical period of pulmonary infection had been surmounted and the spinal-fluid protein had dropped to 211 mg. without clot, the crisis appeared to be past. Unfortunately, an inhalation pneumonia led to sudden death. Autopsy showed the Pacchionian bodies uniformly plugged with amorphous material, which was beginning to show recanalization.[41] There were no adhesions or other cause of hydrocephalus. Spinal-fluid clots and webs are due to the leakage of fibrinogen and fibrin ferment into the subarachnoid space.[31] It is therefore clear that in this case the spontaneously clotting material in the spinal fluid had led to obstruction of the Pacchionian bodies, with resulting external hydrocephalus and papilledema that threatened optic atrophy. Recanalization was greatly delayed. The protein molecules evidently gain entry to the subarachnoid space from the congested nerve roots. In our case the protein from cisternal puncture was 87 mg. per 100 cc. at a time when lumbar puncture gave a value of 222 mg. In a patient of Bassoe[39] who had blurred optic disks the cisternal protein was 25 mg. and the lumbar 2000 mg. The large fibrinogen molecule must nevertheless find its way to the vertex, probably because it cannot be resorbed elsewhere. Our

studies have also shown that in meningitis identical obstruction by fibrin may occur, and although it then tends to recanalize rapidly because of lysis by the concomitant exudate, it may for a time lead to papilledema that requires daily drainage for its relief. In subarachnoid hemorrhage the Pacchionian villi may also be obstructed, but the absence of fibrin and rapid hemolysis usually results in rapid resolution. In this case the blood is probably defibrinated at or near the site of origin.

In order that such medical conditions can be correctly appraised and blindness from optic atrophy prevented, it is essential to study the fluid. However, we are all aware of the dangers of lumbar puncture in cases of space-occupying intracranial lesion. To know when a lumbar puncture should not be performed is extremely important. It must be remembered that *herniation of the brain is the danger* and that periodic bursting headache, dilation of one or both pupils, vomiting and resistance to passive flexion of the neck are the signs of herniation. Lumbar puncture is dangerous in their presence, yet when papilledema has been found in the absence of these signs careful study of the spinal fluid by lumbar puncture with cautious measurement of pressure is therefore vitally necessary. Awareness of the existence of these medical disturbances of intracranial pressure and confidence in correct judgment of the necessity of or contraindications to lumbar puncture are necessary if errors are to be avoided. Loss of vision from inability to localize a nonexistent tumor can be as disastrous as foramen-magnum block following lumbar puncture.

Muscular Diseases

The enormous variety of muscular diseases, comprising entities that range through almost every specialty, have made these conditions orphans of medicine. The natural interest of neurologists in locomotor disability has brought most muscular diseases to their attention. The absence of knowledge of pathogenesis of most of these diseases, however, has hitherto impeded all attempts to find adequate treatment for them. An earlier passion for classification has resulted in a multitude of names, with slight value in estimating prognosis. The rise of clinical interest in electromyography and the demonstrated value of routine biopsy of obscure muscular diseases are, however, gradually providing a more useful type of knowledge. Our own recent studies have led us to a rationale that emphasizes the importance of the power of the muscle cell to produce myofibrils as a normal physiologic reaction to use or injury. Hypertrophy of muscle is an increase in myofibrils in each fiber; atrophy is related to their disappearance. Neural atrophy is at first a gradual reduction in number of myofibrils, but at a later stage a degeneration of the muscle cell in response to situations that normally stimulate myofibril production begins to occur. In muscular dystrophy this property of myofibril production is lacking. Adams, Denny-Brown and Pearson[42] have examined this and related pathologic processes in the whole group of muscular diseases. The absence of such a factor in muscular dystrophy means that the metabolic fault in these diseases should be sought in the chemistry of regeneration and growth of myofibrils rather than in the contraction process.

Regular biopsy has also taught us much about the different types of polymyositis, for myofibril regeneration is not effected in these diseases, which can be divided into types that primarily cause necrosis of the contents of the muscle fibers yet are rapidly repaired and others that appear to be disorders solely or primarily of the interstitial endomysial and perimysial tissue. The latter group respond well to cortisone, and to understand this response we clearly have much to learn about the connective tissues and their reactions and about their relation to the endocrine glands. The importance of regular biopsy is also indicated in a recent case of nonspecific myositis with mental confusion in a woman of fifty-nine at the Boston City Hospital, which was shown by biopsy to be due to toxoplasmosis, finally proved by bacteriologic studies.[43]

The physician trained in neurologic medicine has a natural interest in muscular diseases and muscular pathology, and if he is well informed concerning current endocrine investigations he has much to contribute to the further investigation of these difficult problems.

Conclusions

The nature of neurologic medicine is such that the neurologist is employed primarily as a consultant. There are a number of conditions in which he would prefer to undertake the entire responsibility for management, and in some conditions there is need for constant neurologic supervision. If he can demonstrate general ability in internal medicine his colleagues will be the more willing to transfer the neurologic complications of general diseases to his entire charge. For this reason we have insisted that the neurologist have previous training in internal medicine. There are neurologists who do not approve this attitude, maintaining, for example, that psychiatry is more important to the neurologist than medicine. There are others who claim that neurology should be allotted the entire care of nerve injuries, poliomyelitis and so forth. I have set down my reasons for believing that both these attitudes not only are fallacious but also lead to the deterioration of neurology.

Neurologic medicine faces large problems in its own particular field. Knowledge of neural and cerebral function is increasing daily. Better comprehension of the nature of paralysis and of involuntary movements promises considerable improvement in the treatment of such conditions in the future. Even in hemiplegia, better understanding of the

nature of overaction of reflexes has revealed principles of great importance in retraining in movement.[44] New ideas concerning the equilibria of cerebral control of movements give promise of better understanding of the nature of epilepsy and myoclonus, of spontaneous pains and hyperesthesias. In practice, however, all these conditions are best studied in the clinic, where a broad-based clinical philosophy, sensitized to the infinite variations of disease, has no lack of inspiration.

I have endeavored to outline a philosophy of current neurologic medicine and have chosen some recent activities of the Neurological Unit of the Boston City Hospital to illustrate a changing point of view. This is a declaration of faith rather than a recital of achievements. Neurologic medicine is greater than the sum of the contributions of neurologists, and its problems invite the continued attention of all branches of internal medicine. The increasing need for consultant neurologic services in medical clinics is due to the renewed interest of internal medicine as a whole in neurology and can only be met by men initially well trained in internal medicine. Equipped with a special knowledge of the vagaries of neurologic disorders and their underlying pathology and with a flexibility of investigative technic, the neurologist has no difficulty in holding his own in a changing world. If he is given, and makes good use of, facilities to continue his interest in internal medicine, he has much to contribute. He must forever continue to study clinicopathological correlation, which George Cheyne Shattuck the elder did so much to foster and cherish.

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TREATMENT OF THORACIC AORTIC ANEURYSMS BY THE "PACK" METHOD OF INTRASACCULAR WIRING*

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ANEURYSM of the thoracic aorta is a disease of great antiquity. It was described as early as the sixth century by Aëtius.[1] Ambroïse Paré, the great sixteenth-century French surgeon, was the first to suggest the relation of aneurysm and syphilis, according to Butler.[1] During the nineteenth century and the early part of the twentieth, aneurysms were reputed to occur more frequently in this location than elsewhere in the body. In 1847 Crisp,[2] in a series of 530 cases, found 175 of the thoracic aorta compared to 59 of the abdominal aorta. Klotz,[3] in 1926, reviewing 1000 cases, reported 610 and 108 respectively in these locations. Kampmeier[4] in 1938 reported 1163 cases of aneurysms collected from the records of the Charity Hospital in New Orleans from 1905 to 1935, in which 1038 involved the thoracic aorta and only 95 the abdominal aorta. There seems little question, however, in recent years, that the incidence of thoracic aneurysms is declining,

TABLE 1. *Thoracic Aortic Aneurysms: Massachusetts General Hospital, 1942–1951 (September).*

No. of patients	18
Male	17 (94%)
Female	1 (6%)
No. with syphilis	17 (94%)
No. with arteriosclerosis	1 (6%)
No. of fusiform aneurysms*	23 (96%)
No. of saccular aneurysms	1 (4%)

*Six patients had double aneurysms.

undoubtedly as the result of the control and more adequate treatment of the causative disease, syphilis. Despite this reduction in the frequency of thoracic aortic aneurysms, the condition still exists, as is evidenced by the fact that during the ten-year period from 1942 to 1951 inclusive, 17 patients with syphilitic aneurysms and 1 with an arteriosclerotic aneurysm have been treated by intrasaccular wiring at the Massachusetts General Hospital (Table 1). The purpose of this paper is to report the results of treatment in these cases by a new "pack" method of intrasaccular wiring that has recently been developed for the treatment of abdominal aortic aneurysms[5] and to demonstrate that fusiform aneurysms may be treated by this method as well as the saccular type, despite statements to the contrary in the literature.[6, 7] There was a total of 18 patients with 24 aneurysms (double aneurysms were found in 6 patients). Twenty-three, or 96 per cent, were the fusiform type, only 1, or 4 per cent, being saccular. The location of the aneurysms was as follows: Six, or 25 per cent, were in the ascending aorta; 7, or 29 per cent, were in the transverse arch; and 11,

TABLE 2. *Location of Aneurysms.*

Ascending arch	6 (25%)
Transverse arch	7 (29%)
Descending arch	11 (46%)
Total	24*

*Six patients had double aneurysms.

or 46 per cent, were in the descending arch and aorta (Table 2). There were 17 males and 1 female in the group, or 94 and 6 per cent respectively. Syphilis was the etiological factor in 17 or 94 per cent and arteriosclerosis in 1 or 6 per cent. The ages of the patients ranged from 42 to 73 years with a mean age of 54 years. There were four in the fifth decade

TABLE 3. *Age of Patients.*

No. of Patients	Age
	yr.
4	40–49
6	50–59
7	60–69
1	70–79
18	
Minimum age	42
Maximum age	73
Mean age	54

of life, six in the sixth, seven in the seventh and one in the eighth (Table 3).

The symptomatology in this group of patients was of considerable interest (Table 4). Pain was the

TABLE 4. *Symptoms in 18 Patients with Aneurysms.*

Pain	18 (100%)
Moderate	5 (28%)
Severe	13 (72%)
Dyspnea	13 (72%)
Hoarseness	8 (44%)
Cough	7 (39%)
Dysphagia	6 (33%)
Hemoptysis	1 (6%)

most common symptom, as it was observed in all 18, or 100 per cent, of the patients. It varied in intensity from a moderate degree in 5, or 28 per cent, to a severe and incapacitating form in 13, or 72 per

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cent. Dyspnea was the next most common symptom, occurring in 13, or 72 per cent, of the group. Hoarseness and the characteristic "brassy" type of cough were observed respectively in 8, or 44 per cent, and 7, or 39 per cent, of the cases. Dysphagia occurred in 6, or 33 per cent, and hemoptysis arising from erosion of the trachea by the aneurysm, probably one of the most ominous signs of impending death from rupture of the aneurysm, was seen in 1 patient, or 6 per cent of the group.

The duration of life, according to most writers on the subject, is measured in months after the onset of symptoms from thoracic aneurysms. Kampmeier[4] found in his series that in aneurysms of the transverse and descending arch the average time between the onset of symptoms and death was only 6.4 months, in the descending aorta 8 months and in the ascending aorta 8.9 months. Colt[8] records slightly longer periods — twelve months for the ascending aorta, nine months for the transverse arch and twenty months for the descending aorta. These figures do not, of course, indicate the duration of the lesion, since many may be present for years before they cause symptoms.

The inevitability of death resulting from rupture of the aneurysmal sac or suffocation from pressure by it on the trachea is well recognized. Boyd[9] in 1924 reviewed 4000 reported cases of aneurysm of the thoracic aorta and found that about 52 per cent died from rupture of the aneurysmal sac. Kampmeier[4] in 1938 reported that in 247 patients dying from aneurysm rupture of the aneurysmal sac was the most common cause of death, as it occurred in 98, or 40 per cent. Respiratory obstruction was the next most common cause, occurring in 46, or 18 per cent, and cardiac failure in 29, or 11.5 per cent, was the next most frequent cause. The hopelessness of adequate means of controlling the ever-increasing aneurysmal dilatation is also frequently emphasized in the literature. The various surgical procedures that are applicable to aneurysms of the more peripheral arteries, such as the endoaneurysmorrhaphy of Matas[10] or the more recent operation of aneurysmectomy,[11] cannot be performed for this lesion of the thoracic aorta in the majority of cases. Lam and Aram[12] in 1951 reported the resection of a fusiform thoracic aneurysm of the descending aorta and the insertion of a homologous aortic graft to bridge the defect, but their patient survived only a few months. Since the majority of thoracic aortic aneurysms involve the ascending aortic arch with its great vessels, there seems little likelihood that similar procedures will be applicable in such cases.

The earliest attempts to produce the formation of an intravascular thrombus were made independently by Velpeau[13] and Philips[14] in 1831. They described a method of arterial occlusion by the introduction of needles into the lumen of a blood vessel, later to be withdrawn after a thrombus had formed about them, and suggested that it might be utilized in the treatment of aneurysm. The credit for being the first to advocate and practice the insertion of wire into an aneurysmal sac to be left in place to create an intrasaccular thrombus is given to Moore,[15] an English surgeon. He and Murchison[15] reported this method of treatment in a man of twenty-seven with a syphilitic aneurysm of the ascending aorta. The patient died five days later from sepsis — not a surprising outcome, since this was prior to the advent of antisepsis and asepsis.

The feasibility and the possibilities of this method were recognized by others, however, so despite the fatal issue in the first patient, the method continued to be utilized.[6, 7, 16-19] Various modifications of it were also developed. Ciniselli[20] in 1868 was the first to employ an electrical current to aid in the deposition of fibrin and the formation of a clot by passing it through needles inserted in an aneurysmal sac and later withdrawn. Buressi and Corradi[21] in 1879 reported the use of a galvanocurrent to heat the wire after inserting it through an insulated needle. This method was in vogue for several decades but was finally abandoned because of unsatisfactory results. Colt,[22] a British surgeon, contributed considerable impetus to the wiring procedure by developing a gold-plated steel-wire wisp or umbrella that was pushed into the aneurysmal sac through a trocar. This method yielded a few brilliant results[22-24] but failed in the majority of cases, it is believed, because insufficient wire to stimulate thrombus formation could be inserted. Colt made an important contribution, however, to the wiring procedure, as he demonstrated that a dull finish on the wire, which increased its surface area, was sufficient stimulus to initiate clotting, making electrical heating of the wire unnecessary. Despite an occasional patient benefited, the wiring of aneurysms has been practically abandoned during the last two decades except by Blakemore,[25] because of the almost universally unsatisfactory results of the procedure. His contributions[26] in the field, however, have been outstanding during this period. He developed an electrothermic method of coagulation of aneurysms that has produced a higher percentage of good results in his hands than has previously been reported.

The realization of the inevitable fatal outcome in most cases of aneurysm and the demonstration by Blakemore of the successful treatment of thoracic and abdominal aneurysms, including the fusiform type as well as the saccular type, by his method of wiring (especially since he used greater lengths of wire than had been previously reported) stimulated us to attempt wiring in our cases. Since it was not feasible to duplicate Blakemore's apparatus for electrically heating the wire and impossible to obtain the insulated fine wire he had inserted in the aneurysm, stainless-steel wire, Type 302, 30 gauge, was utilized. It was roughened to increase its sur-

face area, like the buffed-surfaced wire that Colt[22] had recommended. As it is impossible to determine the weakest part of the aneurysmal sac where rupture is most likely to occur, and since our attempts at wiring aneurysms with the Colt wire wisps had demonstrated that with this method it was not possible to insert sufficient wire in most aneurysms to produce the necessary amount of intravascular thrombosis to strengthen the aneurysmal wall, the "pack" method of wiring has been developed, thereby attempting to give support to the aneurysmal sac at all points.

Technic of the "Pack" Method of Intrasaccular Wiring

A review of the earlier wiring attempts at the Massachusetts General Hospital and most of the cases recorded in the literature during the first part of this century has revealed that in most cases only 10 to 20 feet of wire was inserted and in many cases even less. It is believed that this explains, in part at least, the failure of the method, because the desired amount of thrombus formation was not obtained in most of these earlier cases. Such short lengths were used because the wire had to be passed manually by pushing it in, thereby limiting the amount that could be inserted. In addition, a stiffer and larger-gauge wire was necessary in order to be able to introduce it in this manner, which prevented it from coiling satisfactorily and thereby also limited the amount that could be introduced. It may also have been that the operator feared that a larger amount of wire might produce complete thrombosis of the artery, an occurrence that is apparently most unlikely in view of the many hundreds of feet of wire that were used in the cases reported in this article, without producing it. It is of interest in this regard to note that Moore[15] in 1864 stated: "The chief fault, if failure occurred from the manipulation, would doubtless be not introducing enough wire."

Since the principle of the wiring method is to strengthen the wall of the aneurysmal sac at all points by the introduction of sufficient wire to stimulate thrombus formation, it is necessary that a fine wire be used to facilitate its coiling and wide distribution within the aneurysm. Because of the flexibility of the type of wire used in the cases reported here, it was impossible to push it manually through a trocar in sufficient amounts to fill the sac, and it was not until the Blakemore[25] type of wiring trocar was adopted that this difficulty was overcome. The trocar consists of a double needle so constructed that the inner one fits snugly but not too tightly within the outer one. The latter has a caliber of 14 gauge and is approximately 6½ inches in length (Figure 1). A sharp-pointed stylet fits this sheath, by means of which the trocar can be readily inserted into the aneurysmal sac. The stylet is then withdrawn and the inner sheath, which has been loaded with the end of the wire, is inserted into the outer sheath. In order to facilitate the coiling of the wire within the aneurysm, several feet are passed through the inner sheath before it is inserted into the outer one; this length is pulled over a firm edge to make it coil. The wire is then withdrawn until its end is at the tip of the inner sheath. After inserting the latter into the outer sheath the first few feet are passed manually, directing it toward the opposite aneurysmal wall, care being taken not to bend the wire, since this causes

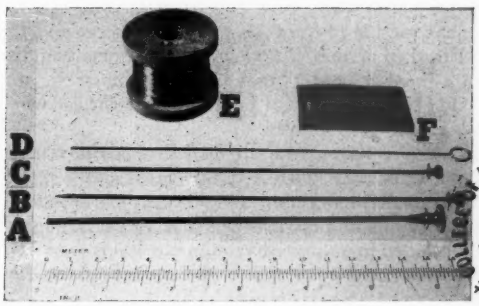

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Figure 1. *Aneurysm-Wiring Apparatus.*
A = The outer sheath of the 14-gauge 6½-inch Blakemore type of wiring trocar. B = The sharp-pointed stylet that fits the outer sheath A and is used to pierce the aneurysmal sac. C = The inner sheath that fits the outer sheath A and is used to pass the wire into the aneurysm. D = The blunt-pointed stylet that fits the wire sheath D and is used to push the end of the wire into the aneurysm after completing the wiring. E = Spool of 200 feet of 30-gauge stainless-steel wire with a diameter of 0.010 inch. F = Fine emery cloth used to roughen wire to increase its surface area.

it to bind in the trocar and interferes with its passage. After this short length of wire has been inserted, it is possible to slip the inner sheath out on the wire; then, grasping both the wire and the end of the inner sheath between the thumb and forefinger, they are advanced into the outer sheath, forcing approximately 6 inches of wire into the aneurysm. This step is then repeated many times, passing this length of wire with each stroke, until all the wire that it is possible to insert has been passed. The direction and the depth of the outer trocar sheath within the aneurysm are changed frequently in order to obtain a wide and even distribution of the wire. Care should be taken not to direct the trocar in the main axis of the aorta, since this may cause the wire to pass into the heart or down the distal aorta. If it is directed toward the opposite wall of the aneurysm, this complication does not occur. In order to fill the sac completely it has been found necessary to reinsert the trocar in several places. The areas that have not been satisfactorily wired can be detected by an expansile pulsation that still persists. When these are located the trocar

is withdrawn; it is then reinserted through the opposite wall of the aneurysm and additional wire inserted. Since it is never possible to make the wire coil at the site of the original puncture, it is always advisable to wire this area by the procedure described above. This expedient has been useful also in controlling bleeding from the puncture wound, especially in thin-walled aneurysms that may have been slightly torn by the manipulation of the trocar. As a rule, however, the bleeding from the trocar puncture sites is readily stopped with finger pressure for a few minutes — or in some cases the sites have been occluded with small plugs of gelfoam. Before withdrawing the trocar each time and at the completion of the wiring, the wire is cut and the end pushed within the aneurysm by means of the blunt-pointed stylet that fits the inner sheath, so that the wire does not protrude from the sac when the trocar is removed.

The wire that has been used is a stainless-steel alloy, Type 302 (18-8),* 30-gauge or 0.010 inches in diameter, containing 18 per cent chromium, 8 per cent nickel and 0.08 per cent carbon. It may be obtained in unlimited amounts in 200-foot lengths at a relatively small cost. The surface of the wire is roughened before sterilization by running it through fine emery cloth, in order to increase its surface area.

TABLE 5. *Length of Wire Inserted in 18 Patients with Thoracic Aortic Aneurysms.*

No. of Patients	Length of Wire *ft.*
3	Less than 100
6	100–200
5	200–300
4	400–500
Minimum	30
Maximum	500
Mean	229

The lengths of wire that were used in the 18 cases are as follows: less than 100 feet in 3 cases; between 100 and 200 feet in 6 cases; between 200 and 300 feet in 5 cases; and between 400 and 500 feet in 4 cases. The minimum length was 30 feet, the maximum 500 feet; the mean amount was 229 feet (Table 5). The larger the aneurysmal sac, the greater the length of wire found necessary to fill it. There was no evidence of obstruction to the blood flow through the aorta or the aneurysm, even in the fusiform type, resulting from the use of these large amounts of wire, despite the innumerable strands that traversed the main axis of the blood stream in the aneurysm. It is significant also that peripheral arterial embolism did not occur in any case.

Methods of Wiring

Two methods of wiring were utilized: the indirect — inserting the wiring trocar through a small skin incision in the thoracic wall without visualizing the aneurysm, and the direct — exposure of the aneurysm through an open thoracotomy incision. The former was performed in 8 or 44 per cent of the cases and the latter in 10 or 56 per cent. Most of the earlier cases were wired indirectly, but on the basis of added experience it is now believed that the direct method permits more complete wiring of all parts of the aneurysmal sac. The chief advantage of the indirect method is that the operative risk is much less if the aneurysm lies near the thoracic wall; as a result it can be performed on the poorer-risk patient, who may be too ill to withstand opening of the chest during the procedure. It is recommended that it be used, however, only in those cases in which the aneurysm lies directly beneath the thoracic wall, since in the more remote ones the trocar may pass through the lung and result in a bronchopleural fistula with a tension pneumothorax, as occurred in 2 cases.

The following are the advantages of the direct method by exposure of the aneurysm through an open thoracotomy incision: The diagnosis of an aneurysm or a thoracic tumor can be determined with certainty, especially in the case that cannot be diagnosed by physical examination and roentgenographic studies; it permits a more adequate distribution of the wire within the aneurysm, because the trocar can be inserted in several places so that the wire may be directed to those areas that are not wired through the initial puncture site; areas in the aneurysmal wall that are thin and are potential sites of rupture may be readily wired (these might be missed by the indirect method); better control of the coiling of the wire is obtained so that there is much less danger of its passing into the left ventricle of the heart or down the descending aorta; important structures such as the lung, the pericardium and the esophagus can be avoided so that there is less danger of a tension pneumothorax, cardiac tamponade and sepsis from transfixing them with the wiring trocar; and control of bleeding from the puncture sites in the aneurysm can be obtained on withdrawal of the trocar as they are under direct vision.

Results

The indirect method of wiring was used in the earlier cases in the group before it was determined that complete packing of the aneurysmal sac was desirable. Despite the disadvantages of this method, however, excellent results were obtained in three patients. One patient was relieved of his symptoms for six years and three months before he died of heart failure at the age of seventy years. Two other patients are alive and relieved, four and one-half and two and one-half years respectively after the wiring; the latter was seventy-three years of age at the time of wiring. The remaining 5 patients wired in this manner all died from rupture of their aneurysms —

*Manufactured by Alloy Metal Wire Company, Incorporated, Prospect Park, Pennsylvania.

in most cases, it is believed, because an inadequate amount of wire was inserted. Two succumbed ten and fifteen days respectively after the wiring, two others after one year and a fifth from rupture and sepsis one year and ten months later. The patient who died on the tenth postoperative day succumbed from cardiac tamponade, at least partly because the wiring trocar, which was inserted through a small skin incision, passed through the pericardium, which had been displaced upward by the enlarging aneurysmal sac. Leakage of blood from the puncture site in the sac and also from a partial rupture of the aorta near its origin caused death from cardiac tamponade. In this patient, direct exposure of the aneurysm through a right thoracotomy incision would have demonstrated this abnormal anatomical relation and the trocar might then have been inserted directly into the sac without entering the pericardium. At the same time, a site for inserting the trocar could have been selected that would have permitted adequate wiring at the weak area in the sac wall, where rupture occurred.

The results of the direct method do not show the alleviation of symptoms or the prolongation of life for as long periods as the indirect method in this group of cases. It is believed this is because complete packing of the aneurysm has been used only during the last two years. It is noteworthy, however, that no patient in whom the wiring was considered adequate has died from rupture when this method was employed. There was one postoperative death on the first day following the wiring in a very ill patient with a huge aneurysm of the descending aorta occupying most of the left pleural space. This patient was probably beyond relief because of the size of the aneurysm, but, in retrospect, the indirect method should have been used because he was so critically ill. One patient, early in the series, died from rupture of the aneurysm one month after wiring, before the packing technic was developed. In this case only 75 feet of wire was inserted; this would now be considered an insufficient amount, in view of the size of the aneurysm. Two patients died from tracheal obstruction six and eight months after the wiring. Both patients had aneurysms of the ascending and transverse arches of the aorta, with compression of the trachea that was not relieved by the procedure. Another patient with a huge aneurysm of the descending arch and aorta died four and one-half months later from heart failure. Five patients are still alive, — 1, two years, 1, one and one-half years, 1, eleven months, 1, five months and 1, three months after wiring, — with marked relief or improvement of their symptoms.

The relief of symptoms obtained in this group of patients by this method of therapy is of considerable interest, since in the 16 patients who survived the wiring 8, or 50 per cent, had complete relief of pain, the most common symptom; 6 or 38 per cent had partial relief; and in 2 or 12 per cent no improvement was noted (Table 6). The relief obtained was most evident in the severe group, since some of the patients who had been incapacitated by the pain were completely rehabilitated and were able to return to their work, which in some cases involved heavy manual labor.

Dyspnea, the next most frequent symptom, observed in 12 of the patients who survived the wiring, was completely relieved in 6 or 50 per cent and partially in the other 6 or 50 per cent; the least improvement was shown in the 2 patients who had marked tracheal obstruction, from which they died in six and eight months respectively. Hoarseness was the next most frequent symptom, as it was observed in 8 or 44 per cent of the surviving patients. It was completely relieved in 3 or 38 per cent and was somewhat improved in the other 5 or 62 per cent. The characteristic "brassy" type of cough was observed in 6 or 38 per cent of the survival cases. It disappeared in 3 or 50 per cent of the patients and showed only slight improvement in the other 3. Dysphagia was relieved in 2 or 40 per cent of the 5 patients who survived the wiring procedure. It was partially relieved in the other 3 or 60 per cent. It is of extreme significance that hemoptysis from erosion of the trachea by the aneurysm, which was observed in one of the patients, ceased after the wiring and that the patient is still alive approximately one and one-half years after operation, since if untreated this patient probably would have died from rupture of the aneurysm in a matter of days or weeks.

Table 6. *Relief of Symptoms in 16 Surviving Patients.*

	No. of Patients	Complete Relief	Partial Relief	No Relief
Pain	16 (100%)	8 (50%)	6 (38%)	2 (12%)
Dyspnea	12 (75%)	6 (50%)	6 (50%)	—
Hoarseness	8 (44%)	3 (38%)	5 (62%)	—
Cough	6 (38%)	3 (50%)	3 (50%)	—
Dysphagia	5 (31%)	2 (40%)	3 (60%)	—
Hemoptysis	1 (6%)	1 (100%)	—	—

Table 7. *Causes of Death.*

	No. of Patients
Early deaths (postoperative)	
Heart failure	1
Rupture of aorta with cardiac tamponade	1
Operative mortality	2 (11%)
	4
Late deaths	
Rupture of aneurysm	5
Tracheal obstruction	2
Heart failure	2
Total	9

In addition to relieving the symptoms of aneurysm, the chief purpose of this form of treatment is to prolong life by preventing rupture of the aneurysm. That this was attained in some patients is probable, but unfortunately this was not true in all cases. There were 2 operative deaths, a mortality rate of 11

per cent — one from heart failure and the other from rupture of the ascending aorta with resulting cardiac tamponade (Table 7). Nine patients or 56 per cent of those who survived the wiring procedure died at periods varying from fifteen days to six years and three months after wiring. Five or 55 per cent of the deaths resulted from rupture of the aneurysms; 2 occurred within one month of the wiring and without question were failures. The third patient lived one year and ten months before succumbing to sepsis and rupture. It is believed that his life was prolonged by the procedure; if his condition had not been complicated by sepsis within the wired aneurysm he probably would have survived longer. As a result of this complication all patients now routinely receive prophylactic penicillin therapy both pre- and postoperatively. The other 2 patients died at the end of one year, from unknown causes but probably from rupture of the aneurysms, since they were among the first operated on, and relatively small amounts of wire were utilized in their cases. It is important to note that in these 5 patients who

TABLE 8. *Length of Life in 16 Patients Who Survived Wiring.*

	ALIVE	DEAD
No. surviving 6–7 years	0	1
No. surviving 4–5 years	1	0
No. surviving 2–3 years	2	0
No. surviving 1–2 years	1	3
No. surviving 1 year	1	2
No. surviving less than 6 months	2	3
Totals	7	9

died after wiring from rupture of their aneurysms the "pack" method was not carried out in 4 cases. According to present standards, insufficient wire was inserted to fill the aneurysmal sacs completely in these cases, as only 40, 75, 115 and 150 feet respectively were used in them. The fifth case was wired indirectly without exposure of the aneurysm; even though 300 feet of wire was inserted, it is believed that under direct vision a more complete filling of the sac could have been performed and rupture prevented.

Two of the nine deaths resulted from subsequent tracheal obstruction, at six and eight months respectively. Both patients had large multiple aneurysms that had produced this condition prior to wiring. Some improvement followed the procedure, but it was not sufficient to be noteworthy. It is believed, however, if they had been seen and treated earlier before the aneurysms had become so large the results would have been much better. In both cases the aneurysms were of the transverse arch; because of their location and size, it is doubtful that benefit can be obtained in the future for similar cases by this type of treatment. It cannot be stressed too strongly, therefore, that wiring should be performed earlier in the course of the disease before the aneurysms become so large that they produce tracheal obstruction.

The remaining 2 patients died from heart failure. One had multiple aneurysms; he survived four and one-half months, but his symptoms were in great measure relieved. Treatment had been delayed too long in this case. The other patient lived for six years and three months, completely relieved of his symptoms of aneurysm, dying at the age of seventy. It is believed that this case without question represents a successful result.

Seven patients are still alive at this time, from three months to four years and five months after wiring (Table 8). In view of the statistics on life expectancy after symptoms develop from thoracic aneurysms — in most instances a matter of less than a year[4, 8] — it is believed that 5 of these 7 patients have definitely had their lives prolonged by the procedure, since one is alive and well (as far as the aneurysm is concerned) at four years and five months; a second, at two years and eight months; a third, at two years; a fourth, at one year and five months; and a fifth at one year who was practically bedridden at the time of the wiring. The remaining 2 are alive, three and six months after wiring, which is too short a period to determine the value of the procedure in view of the natural life expectancy of aneurysm.

In summarizing the results, it can be stated that the symptoms of the disease were relieved in the majority of cases and that, although life was not lengthened in all cases as much as could be hoped for, the wiring did prolong it in 11 or 61 per cent of the group of 18 patients (Table 8). If these cases are arranged according to the length of survival since the wiring, it is to be noted that 1 survived six years and three months and then died of heart failure; 3 are alive at four and one-half, two and one-half and two years respectively; 1 is alive and 3 are dead at between one and two years; 1 is alive and 2 are dead at the end of one year; and 2 are alive and 3 are dead at less than six months after the wiring. Since the life expectancy in this group of patients without wiring, according to available statistics, is less than one year, it is believed that the lives of these 11 patients were prolonged for one year to six years and three months. Furthermore, it is believed that if all cases had been adequately wired by the "pack" method the survival statistics would have been even better, especially in those in whom the wiring was inadequate and who died from rupture of the aneurysms.

CASE REPORT

A. M., a 47-year-old man, was first admitted to the Massachusetts General Hospital on June 2, 1948, for the treatment of late cardiovascular syphilis; at that time a diagnosis of a syphilitic aneurysm of the descending arch of the aorta was made. He stated he had enjoyed good health until 1939, when he first experienced a dull, steady pain in the left side of the chest near the inferior angle of the scapula that came on while he was shoveling snow. It lasted 2 hours and disappeared. He was fairly well until the winter of 1943, when

his pain recurred spontaneously. His local physician gave him some electrical treatment, with relief. Since then, however, the pain had continued off and on. It was worse in wet weather. He described it as a dull, steady, nagging pain varying in intensity from moderate to severe. At times it was a pounding sensation and was aggravated by sneezing. At this time he had no dysphagia. Past history was noncontributory. He was born in the Cape Verde Islands and had been in the United States since 1920. He denied any venereal diseases. He was a laborer and at that time was working in the cranberry bogs.

Physical examination revealed a rather thin, well-developed middle-aged man. The pupils were equal and reacted to light and accommodation. There was slight enlargement of the heart and of the retromanubrial dullness. The blood pressure was 112 systolic, 68 diastolic.

The electrocardiogram showed a normal tracing. The urine, of specific gravity 1.010, was negative for sugar and albumin. Examination of the blood disclosed a hemoglobin of 15.0 gm. and a white-cell count of 6100, with a normal differential. Blood Wassermann and Hinton tests were positive. The spinal-fluid total protein was 22 mg. per 100 cc., the gold sol 0001111000, the sugar 70 mg. per 100 cc. and the chlorides 122 milliequiv. per liter. X-ray examination on June 3, 1948, was reported as follows: "Both lungs are clear. There is a soft tissue mass present in the upper posterior mediastinum. This mass is smoothly rounded and shows no calcification. On fluoroscopy it shows slight pulsation but this appears to be mainly transmitted. It is continuous with parts of the aorta and cannot be separated from the arch of the aorta. There is anterior and left displacement of the esophagus and trachea, and a slight obstruction due to pressure of the esophagus. There is erosion of the anterior margins of the bodies of the 4th, 5th, 6th and 7th vertebrae. The appearance is consistent with a large aneurysm just distal to the arch of the aorta."

The patient was given 6,000,000 units of penicillin by intramuscular injection in divided doses. He was discharged home on June 24, 1948, on potassium iodide by mouth.

He returned to the Out-Patient Department Clinic on January 5, 1949, complaining that he was unable to sleep because of severe pain in his left chest. A repeat roentgenogram of the chest on January 18 revealed slight enlargement of the aneurysm with some obstruction to barium passing through the esophagus (Fig. 2).

Second admission. The patient was readmitted on September 13, 1949, because since his first admission his condition had gradually worsened. For the past year, the pain had been much more severe. Four months before this entry he developed severe dyspnea and orthopnea. The slightest exertion caused him to choke up. He had to sleep on three to four pillows. He also developed severe dysphagia during the past 4 months; he could now swallow only liquids. As a result he had lost 35 pounds in weight during the last few months.

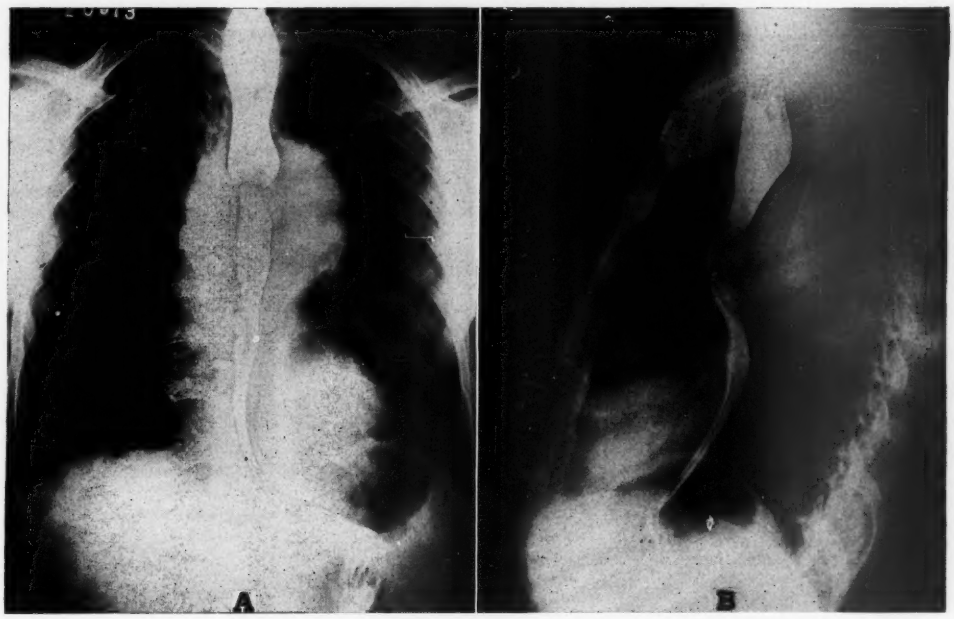

FIGURE 2. *Retouched Photographic Reproductions of Preoperative Roentgenograms Taken January 18, 1949.*
A = *Anteroposterior roentgenogram, demonstrating the aneurysm above the heart in the superior mediastinum and the partial obstruction of the esophagus to the passage of a suspension of barium.* B = *Lateral roentgenogram, demonstrating the aneurysm in the posterior mediastinum, the displacement of the esophagus forward by it, the partial obstruction of the esophagus and the marked erosion by the aneurysm of the bodies of the 4th, 5th, 6th, 7th and 8th thoracic vertebras.*

Physical examination revealed an emaciated man lying propped up in bed in severe pain. There was little change in his physical signs, but the heart was a little more enlarged and there was a fairly loud diastolic aortic murmur. There was a slight pulsation posteriorly in the region of the vertebral spine near the 5th and 6th ribs. There was an area of hyperesthesia over the distribution of the 4th, 5th and 6th intercostal nerves. A marked tracheal tug was noted on this admission. He had no hoarseness or brassy cough. The blood pressure was 130 systolic, 75 diastolic. Laboratory examination of the blood revealed a hemoglobin of 12.5 gm. and a white-cell count of 8100. The urine was negative for sugar and albumin.

Sixty mg. of codeine sulfate, by subcutaneous injection, was necessary to control the pain. A transthoracic exposure of the aneurysm with intrasaccular wiring by the "pack" technic was advised.

An operation was performed on September 17, 1949. Under endotracheal ether anesthesia, with the patient lying on his right side, the greater portion of the left 6th rib was resected. A large, pulsating aneurysm about 10 cm. in diameter was found arising from the descending arch and the first portion of the descending aorta. The upper portion of the lower lobe of the lung was adherent to it. This was carefully dissected away to expose the aneurysm. The posterior wall of the aneurysm was embedded in the thoracic wall and the left anterior surfaces of the bodies of the 4th, 5th, 6th, 7th and 8th vertebras. The wiring trocar was inserted in the anterior part of the aneurysm. There was no intravascular thrombus, since the wall was very thin, and bleeding occurred from the trocar almost as soon as it had pierced the aneurysmal sac. Four hundred and ninety feet of 30-gauge stainless-steel wire that had previously been roughened was inserted, in three sections of 200, 150 and 140 feet each. This completely filled the aneurysmal sac. After the end of the last section of wire had been pushed into the aneurysm, bleeding from the trocar puncture sites stopped spontaneously. The expansile pulsation in the aneurysm seemed much diminished after wiring. The lungs were reinflated. The thoracic incision was closed with interrupted sutures of silk. No drainage was instituted. The anesthesia for the operation required 3 hours and 50 minutes. The operating time was 2 hours and 55 minutes. The patient received two blood transfusions during the operation. His systolic blood pressure ranged from 120 to 105 systolic and 70 to 60 diastolic. Postoperative x-ray films revealed that the wire was neatly coiled and limited to the aneurysmal sac (Fig. 3).

The patient made a satisfactory convalescence. The pain had disappeared by the second postoperative day. He received an additional 5,300,000 units of penicillin in divided doses intramuscularly during his postoperative period. He was discharged home on the 10th postoperative day. The incision healed *per primam*. He returned to work 2 months after his operation and has remained at work since then. He states that he has no pain and has no difficulty in swallowing; he can eat a normal diet.

FIGURE 3. *Retouched Photographic Reproductions of Roentgenograms Made after Wiring: Taken September 23, 1949.*
A = *Anteroposterior roentgenogram, demonstrating the many coils of the 490 feet of wire filling the aneurysmal sac.* B = *Lateral roentgenogram, demonstrating the coils of wire occupying the space of the bodies of the 4th, 5th, 6th, 7th and 8th thoracic vertebras.*

Discussion

The result of the wiring procedure in this patient has been extraordinarily satisfactory. The relief of pain was spectacular and the disappearance of dysphagia gratifying. From a condition of complete incapacitation and invalidism requiring narcotics for sedation, he has returned to full work as a laborer and is still well 27 months after wiring. It is of some interest, also, that a repeat x-ray film taken one year after the operation revealed some evidence of bone regeneration in the body of the 7th dorsal vertebra and in the 6th rib. Of extreme importance is the fact that the roentgenologists were able to demonstrate only a transmitted pulsation in the aneurysm, never an expansile one. The diagnosis of thoracic aortic aneurysm, therefore, should not rest with the fluoroscopic examination, since in many cases, as in this one, an expansile pulsation is not always demonstrable. The prognosis in this case is difficult to make, but it is hoped that with the satisfactory wiring, in which 490 feet of wire was used, and with the administration of 11,000,000 units of penicillin to control the syphilis,

he will continue satisfactorily for many years. Additional wiring may be necessary at a later date if the aneurysm enlarges.

Finally, it is believed that the intrasaccular wiring procedure utilizing the "pack" method is the best form of treatment for aneurysms of this type. Their location in the arch of the aorta and the invasion of the bodies of the vertebras by the aneurysm, with the result that these bones are actually a portion of its wall, make it impossible to resect them or perform an endoaneurysmorrhaphy; furthermore, the application of cellophane sheets on the exterior of the aneurysm would be of little or no value, as none of the sac wall that is causing the symptoms can be visualized.

Conclusions

The majority of thoracic aortic aneurysms are syphilitic in origin.

If untreated, they represent a fatal condition in the majority of cases; death usually occurs from rupture of the aneurysm or suffocation due to compression of the trachea within a year after the onset of symptoms.

Eighteen patients with thoracic aortic aneurysms have been treated by the intrasaccular wiring method during the past decade, utilizing a new "pack" technic, in the majority of cases, to insert 100 to 500 feet of stainless-steel wire.

Fusiform aneurysms as well as the saccular type may be treated by this method.

The wiring is best accomplished by direct exposure of the aneurysm through an open thoracotomy incision.

Though not the ideal treatment, the "pack" method of wiring aneurysms has resulted in the relief of symptoms in the majority of the patients and in the prolongation of life in a gratifying number.

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MYASTHENIA GRAVIS: REPORT OF A CASE WITH EXOPHTHALMOS, WITHOUT HYPERTHYROIDISM, RELIEVED BY NEOSTIGMINE

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IDAHO FALLS, IDAHO

MYASTHENIA gravis has frequently been described as a clinical entity. It is a disease characterized by abnormal skeletal-muscle fatigability. The cause is unknown. The myoneural junction seems to be the site of the main abnormal reaction. Insufficient acetylcholine or increased motor end-plate resistance appears to block incoming nerve stimuli. Neostigmine, physostigmine, diisopropyl-fluorophosphate and other anticholinesterases decrease this fatigability and may allow almost normal muscular strength. In recent years thymectomy has given occasional good results, and some cures have been reported. This procedure seems to increase the amount of transmitter substance at the myoneural junction. The symptomatology and diagnosis are fairly well agreed on. A recent review of the subject, with current references, was made by Viets,[1] with a discussion of some of the newer aspects of treatment, including thymectomy.

FIGURE 1. *Appearance on Initial Examination and When Not Under Neostigmine Therapy.*

MYASTHENIA GRAVIS AND HYPERTHYROIDISM

Myasthenia gravis with hyperthyroidism and exophthalmic goiter has been reported. Eaton is quoted by McEachern and Parnell[2] as stating that 6 per cent of myasthenic patients studied at the Mayo Clinic have had coexistent hyperthyroidism. McEachern also reports, from 8 cases, that these two conditions were found together only in women and that an inverse relation generally existed between the two conditions, so that when the hyperthyroidism increased the myasthenia gravis was improved. When the hyperthyroidism was decreased by operation or by antithyroid therapy, the myasthenia gravis became worse. In 3 of 8 cases, however, this relation was not found. The first case of myasthenia gravis with exophthalmic goiter was reported by Rennie[3] in 1908. In 1941, Kowallis, Haines and Pemberton[4] reviewed the literature and found 10 additional cases. They added 3 cases and 1 case of adenomatous goiter with hyperthyroidism, combined with myasthenia gravis. In one of their cases relief of both the hyperthyroidism and the myasthenia was obtained by subtotal thyroidectomy.

Thorn and Eder[5] again reviewed the literature in 1946 and stated: "The combination of myasthenia gravis and Graves' disease is rare. To date, six cases have been reported." They added 2 cases.

Greene[6] described an additional case in 1949 with extensive eye signs in which there was no reciprocal relation between the hyperthyroidism and the myasthenia gravis. Another case was reported by Taylor and Large[7] in 1951. Other cases undoubtedly have been seen but not reported.

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Ocular Signs

Eye signs in myasthenia gravis are fairly common. Mattis is quoted by Lisman[8] to the effect that there were ocular signs in 96 per cent of all cases at some time during the disease. Ptosis is the most frequent symptom, being present in 46 per cent of all cases. Diplopia was present in 34 per cent. Eye-muscle weakness has commonly been described. In some cases, this weakness has disappeared under neostigmine therapy. Some authors have regarded those paralyses that do not disappear under neostigmine therapy as due to some other disease or to some complication such as hyperthyroidism.

The present case is reported because it concerns a patient with typical myasthenia gravis in whom exophthalmos was present that was relieved by the administration of prostigmine. This apparently has not been previously reported. Walsh[9] states: "Some years ago, Dr. A. M. Harvey stated that at Vanderbilt they had seen exophthalmos relieved by injection of prostigmine. I subsequently used the drug on a good many such cases, a great majority of which did not have any evidence of myasthenia gravis. In none of these cases was there any reduction of the exophthalmos whatsoever. Your case, consequently, represents the first such proven case that has come to my attention." This patient also had diplopia. There has been no evidence of hyperthyroidism in this case, hence the exophthalmos seems to be a purely myasthenic phenomenon.

Figure 2. *Appearance Five Minutes After Subcutaneous Injection of 1.5 Mg. of Neostigmine.*

Case Report

C. C., a 31-year-old woman, was first seen because of a skin rash. At the time of the first examination she was so weak that she was unable to walk across the room unaided and was largely bedridden. Her condition had been diagnosed as uncomplicated myasthenia gravis at the Mayo Clinic in 1936. At that time her basal metabolic rate was +1. Laboratory examinations, including urinalysis, blood count, chest x-ray films and so forth, were negative.

She was well until the age of 14. At that time she had some slight enlargement of glands in her neck and a slightly rapid pulse. Her menstruation began just before she was 15 years old. There was no exacerbation of her symptoms at that time. There was a slow progression of her weakness over the next few years that was most noticeable during strenuous activity. At about 18 years of age she began to notice some effect on her walking. She then had slight crossing of the eyes, with difficulty in control of their movements, and some double vision. This was worse at the end of the day. Also at the age of 18 she noted that she was always tired when she woke up. This feeling progressed slowly into the feet and then into the arms. After a rest she could walk normally but would later need to rest again. This condition became gradually worse; she noticed that it was intensified before her menstrual periods. By the age of 20 her eyes were protruding constantly. She had no difficulty with movements of the eyelids, but chewing and lip control were difficult. Thereafter she noted difficulty in holding her head up. After the age of 21 she was generally confined to the house. She had pneumonia almost every winter — sometimes two to three times. She began taking very small doses of neostigmine but noticed no effect from them and subsequently discontinued the drug. (In retrospect, these doses were extremely small and could not have been expected to produce much improvement.)

At the time of our initial examination, she was resistant to the idea of using neostigmine because she had tried it without benefit. Her examination showed a skin rash about the neck that subsequently proved to be due to sensitivity to milk. Her general physical examination, aside from the extreme weakness, was negative except for the eye findings. There was some turning in of the right eye, with marked widening of the palpebral fissures and what appeared to be marked exophthalmos. There was diplopia.

She was given 1.5 mg. of neostigmine by subcutaneous injection. Within 5 minutes her exophthalmos had disappeared completely and her eye muscles were completely balanced. She was generally strong enough to walk up and down the stairs without help, which she had not been able to do for years. When she was under neostigmine therapy, glasses

that had previously corrected her refractive errors were no longer effective.

Since that time, she had taken 13 to 14 neostigmine bromide tablets (15 mg.) per day and is able to carry on a nearly normal life. She can walk, dance and perform most physical activities, including all kinds of housework.

Discussion

The mechanism of this particular reaction is not known. Exophthalmos due to enlargement of the eye muscles has been described. It is understandable that an increase in orbital contents from any cause could produce exophthalmos, but a transient exophthalmos based on a muscle weakness is more difficult to explain, especially when it does not usually occur even in cases in which eye muscles are extensively involved. Walsh,[9] in a personal communication, stated that in view of the accompanying photographs it is difficult to rationalize this change as a result of neostigmine therapy. He concedes that the eyes come forward as a result of atony of the extraocular muscles but in the usual case proptosis is not present.

It has been stated that this might not be true exophthalmos but only a widening of the palpebral fissures. Clinically, the appearance is so striking that most clinicians would certainly call it exophthalmos.

Summary

A case is presented of typical myasthenia gravis without hyperthyroidism but with exophthalmos that was promptly relieved by the administration of prostigmine.

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MEDICAL PROGRESS

ASTHMA IN CHILDREN

A Follow-Up Study of 688 Patients After an Interval of Twenty Years (Concluded)

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BOSTON

Negative Skin Tests

The first installment of this paper described the study of 370 children with asthma who were seen before age thirteen and showed positive skin tests. This section deals with a group of 79 cases (48 boys and 31 girls) comparable except that skin tests showed no reaction to any of the common foods or dusts. Of these 79 cases, 49 are "cured"; they include 32 boys and 17 girls who have had no asthma since their teens. Their asthma began at average age 3.6 and they were first seen at average age 6.8; their asthma cleared at average age 14.4, and they were followed up to average age 27.8.

In 25 of the cases, the dominant feature of the history was head colds and bronchitis. When these patients were first seen around 1925, the diagnosis of "bacterial asthma" had been made, a diagnosis difficult to confirm since skin tests with bacterial products were never helpful. Infection in the tonsils had been considered, and the removal of tonsils and adenoids had been accomplished in 17 cases, but without benefiting the asthma. Tonsillectomy was advised in another 5 cases; in 2 the relief of asthma could be dated to the operation. In one case the adenoids were important:

J. C., Jr., a boy of 7 with asthma since age 5, had already had his tonsils removed. His cure at age 9 followed a secondary operation for removal of adenoids. (There was no change in his environment.)

In 10 other cases, however, the circumstances under which the attacks began and ended or the results of simple clinical experiments, like getting rid of the cat or dog or changing the pillow or mattress, made it evident that despite the negative skin tests allergy to some dust in the environment was important. For these cases the term "asthmatic bronchitis" seems correct.

J. B. A., a 4-year-old boy, had very large tonsils, which were removed promptly; his asthma cleared, with no further trouble up to age 22. However, the family cat was removed at the same time. The skin test to cat hair was negative, but once previously the asthma had cleared when the old cat died and recurred when a new cat was brought home.

Five of the 10 patients in this group lost their asthma when they moved — 1 to Arizona, the others to different houses. In the other 5, asthma disappeared as soon as a source of dust was taken

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away — the dog or the cat in 2 cases and the kapok mattress or pillow in 3 others.

Finally, in a third group of 14 cases no good appraisal of the original diagnosis can be made, and the evidence for an allergic factor is doubtful at best. It is interesting that in 3 cases the mother was aware that fatigue or excitement, by itself and without a new infection, could precipitate an attack.

Here, therefore, are 25 plus 14, or 39 out of the 49, "cured" patients in whom the factor of allergy was absent or at least undemonstrable. Since their ultimate relief was not concerned with the principles and methods of clinical allergy, one has to reconsider the term "asthmatic bronchitis." The concept has been that "new colds lower the threshold to make a slight degree of allergy effective." Here, however, are patients who became well without any change in environment or diet and without being desensitized to anything. Most of them declare that "when I got over my head colds my asthma did not recur." The experience of this larger group suggests that colds may of themselves cause asthma, that the factor of allergy is not always important, even in "asthmatic bronchitis," and that the finding of negative skin tests need not be surprising. The mechanism of this variety of asthma needs further study. In spite of the difficulties with the diagnosis of "bacterial asthma," it is possible that an allergy to infection, caused by bacteria or viruses, may really exist to produce reactions of the immediate urticarial type in patients who have the capacity to develop sensitiveness.

Treatment, in the form of stock vaccines, was given to a number of these children, usually with considerable benefit, in that the attacks became less severe and less frequent. The follow-up report shows, however, — and all too clearly, — that the complete cessation of attacks occurred some time (usually several years) after this treatment had been omitted, and one cannot ascribe "cure" to any specific factor.

As happens in the other groups of asthmatic children, there are patients (13) who have recovered from their early asthma but now have some other manifestation of allergy. There are 12 with hay fever, the symptoms being mild in all and only 2 patients needing treatment. New skin tests have not been reported. One "child" has eczema, as follows:

> J. H. H., Jr., had "bacterial asthma" with negative skin tests at age 9. He recovered at age 15, had a short recurrence at age 19 and after that developed eczema, which he had not had since infancy. At age 40 the report says: "No more asthma, but the eczema is still bad."

Seventeen patients whose asthma occurred only with colds still have mild trouble at average age 32.6. In one case (F. M. T., Jr.) skin tests repeated at age twenty-eight were found positive. His record gives no clue that he was different from the others in this group. The twin girls (E. and S. B.) are interesting. One started her wheezy colds at age three. After marriage she had a "terrible time" in Texas but was much better in California. Still, however, she must use her inhalant spray at times — up to age thirty-six. If asthma changes with environment, the fact means allergy. The other twin began at age nine. Her story is much the same, except that her asthma has never been severe; she did not go to Texas. At age thirty-six, however, she still occasionally uses a spray.

Deaths

Eleven of the 449 patients have died. Two boys were killed in military action. A girl of sixteen was killed in a plane crash. Four patients died of intercurrent disease. A girl with horse asthma became a nurse and was free of asthma and well during her training but died from endocarditis at the age of twenty-nine. A boy of eighteen died of "pneumonia." The circumstances are unknown; it could have been asthma. Two patients died of cancer — a "girl" of twenty-three whose asthma had never been severe, and a "boy" of thirty who had suffered all his life from allergic asthma and eczema, sometimes in severe attacks, but who had learned to give himself adrenalin and was able to live a normal life.

Four of the 11 patients died, presumably, of asthma. A boy aged eighteen had episodes of severe asthma all his life and finally had a "heart attack." Another boy, aged twenty, sensitive to animals, had a similar history, but his death was considered due to "bronchopneumonia." A girl, aged twenty-one, with multiple sensitivities, "went from pillar to post taking up with any kind of treatment that promised relief" and finally died "of heart failure following a severe attack of asthma." Finally, a woman, aged thirty, was in a hospital where it is alleged that "they put her to sleep for a week so that nature might heal — and she never woke up!" She had had all types of treatment by several doctors. Skin tests had shown positive reactions to animals, foods and pollens. During her pregnancy, at age twenty-five, she had had no asthma. When last seen at age twenty-seven, she was having a severe attack; she was exhausted and apprehensive, but she had responded well to treatment and general care. The serious aspects of her case had been appreciated, but her death was not expected.

Discussion

About a third of all children with asthma will "outgrow" their symptoms at the average age of fifteen. The animals, foods and pollens and the various house dusts that initially caused their symptoms cease to be harmful. Skin tests to these same substances have been repeated in a few cases and a positive reaction found to persist; hence the word "cure" must be used cautiously. The age at

"cure" averages 14.7 years and varies from five to thirty because the cessation of attacks usually depends on the elimination of the cause. Whether the cat is disposed of early or later depends first on the conviction of the physician and later on that of the patient. Flensborg[5] lays some stress on this, saying that attacks cease in girls before they do in boys. We see little difference in the sexes (Table 2). Table 3 gives the average ages in all the 138 "cured" cases at the times of onset, first visit, cure and follow-up. The figures are remarkably uniform for all the groups, but one must bear in mind that these are average figures that do not reveal the actual wide ranges. Asthma is not "outgrown" at any specific age.

Another 20 per cent of the children, now in their late twenties, are quite well, but they know that they are still sensitive to dogs, cats or kapok pillows and will have trouble unless they continue to avoid these specific things. Some of them recognize that the dust of certain houses or environments can still cause trouble. They are "relieved but still sensitive."

Finally, there is another 20 per cent or more who are now about age thirty and have little if any asthma but do have some other manifestation of allergy — usually hay fever. This means that 30.7 plus 19.3 plus 21.4, or 71.4 per cent of the children, expectedly become free of asthma by about age fifteen.

About a quarter (26 per cent) of the children still have some trouble after age fifteen, but in only 10.9 per cent is this severe. In only 2 per cent of all cases have the attacks been severe enough to require treatment in hospitals. Eleven have died (2.4 per cent), but they died of asthma in only 4 cases (0.8 per cent of the total series).

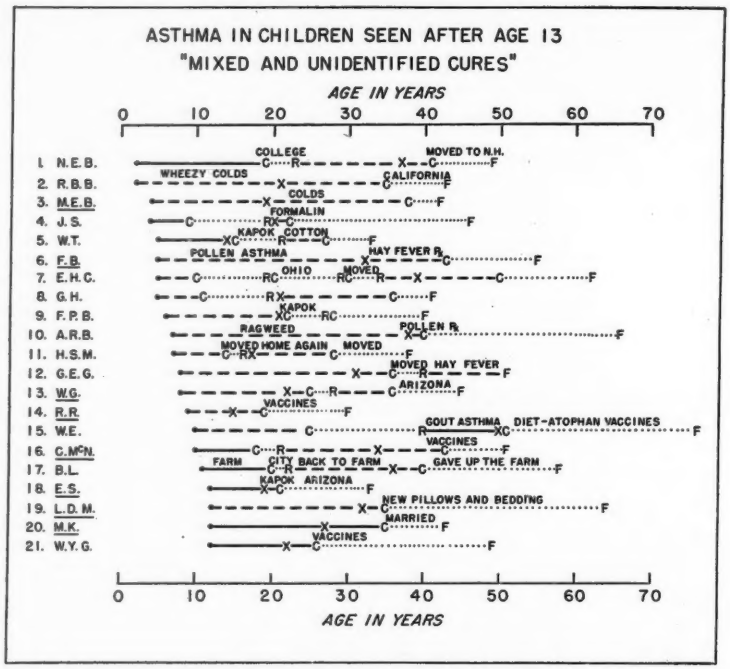

FIGURE 3. *Asthma in Children Seen After the Age of Thirteen: "Mixed and Unidentified Cures."*

Each line represents the progress of a patient and begins at the age of onset. Solid lines represent persistent symptoms; dashes are attacks; the dotted lines represent clearance of asthma. X = *Age at time of first visit;* C = *"Cure" of asthma (or clearance);* R = *Recurrence of symptoms, whether of asthma or of hay fever;* F = *Follow-up; underderlined initials = Girls.*

The interesting group is that in which a new form of allergy, usually hay fever, has developed. In most cases this hay fever has followed the asthma directly. At the first visit the child was found skin sensitive to a variety of substances, including foods as well as dusts, but his history indicated that only one or two of these items was clinically important. The other tests were set aside as "potential" factors, and in some of the cases these later became real factors. The change in the direction of sensitiveness from foods in early childhood to animals later and then to pollens in adult life shows that the essential lesion is not the particular allergy but the capacity to develop sensitiveness.

In a few cases the new sensitiveness was new. The original asthma cleared and then, after the patient had been entirely well for as long as fifteen or twenty years, a new allergy appeared. That the time between cure and recurrence can be as long as this is important. Since this time has been over fifteen years in several cases, it is clear that the long period of follow-up has been important and that observations based on shorter periods may be misleading. In the same sense, one must recognize that recurrences may occur after intervals even longer than twenty years.

What about the different food and dust substances? Does the outcome depend on the direction of the sensitiveness? When the 499 cases are separated into five groups, according to the approximate cause of asthma, the number of cases in each group is hardly large enough to make percentage figures reliable, but trends are discernible. The patients sensitive to animals have done well, because of the ability to recognize and remove the exciting factor. Only 17.5 per cent are still in trouble, and in only 6.1 per cent is this trouble serious. The food patients have lost their clinical sensitiveness entirely in a high proportion (44.4 per cent). Pollens act differently; the sensitiveness, once established, tends to persist, so that after twenty years many patients still have symptoms, occasionally severe. "Mixed and Unidentified" is the larger group in which the figures are about average — as expected. The group with negative tests shows the best results of all, and the results mark it as different from other groups. If bacteria do cause asthma, recovery could be explained by the final development of a true immunity to replace the allergy. As soon as the skin tests can be repeated in these test-negative cases, new information may be obtained, but in any event more knowledge of "bacterial allergy" is needed.

On the whole, this follow-up study of those 449 children with asthma who were first seen in childhood gives a fairly accurate indication of what happened to them up to about age thirty. What happens after that cannot as yet be told in figures, but certain observations on other patients whose asthma began in childhood but who were not seen until some years later serves as a check on the first study.

Asthma in Childhood but Not Seen Until the Age of Thirteen

The title itself suggests a more persistent form of asthma: a selected rather than a natural group of cases. Table 4 summarizes the additional group of 239 older patients. It can be compared with Table 1. The total figures are smaller than in Table 1. There is a higher proportion of animal cases than in the younger group. There are fewer food cases, as might be expected from the deductions drawn above. There are more pollen cases — also as expected. The miscellaneous group is about the same relative size; the group called "Negative Tests" is smaller, as expected.

Table 4. *Original Classification and Present Status of Patients First Seen After the Age of Thirteen.*

Original Cause of Asthma	Total	Cured	Relieved; Still Sensitive	Relieved; Other Allergy	Mild Asthma	Severe Asthma	Severe Asthma in Hospital	Dead
Animal	76 (31.8%)	10	45	4 (2 polypoid sinusitis)	2	13 (3 polypoid sinusitis)	0	2 (1 died of asthma)
Foods	12 (5.0%)	4	5	0	0	3 (2 polypoid sinusitis)	0	0
Pollens	21 (8.4%)	10	0	5	3	3	0	0
Mixed and unidentified	97 (40.5%)	21	11	8	19	35 (5 polypoid sinusitis)	0	3 (2 died of asthma)
Negative tests; "bacterial"	33 (13.8%)	7	0	2	5	12 (2 polypoid sinusitis)	0	7 (1 had polypoid sinusitis; 3 died of asthma)
Totals	239 (100%)	52 (21.7%)	61 (25.5%) 55.2%	19 (8.0%)	29 (12.1%)	66 (27.6%) 44.7%	0	12 (5.0%)

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End results are interesting. Only a little over half of these older patients did very well, whereas in the younger group 71 per cent did very well. The development of other allergies in addition to, or supplanting, the asthma was much less in the older group.

Patients in trouble were much more numerous in this older group, — 27.6 per cent as against only 10.9 per cent in the younger series, — and more of the patients had died. Six of the 239 older patients have died of asthma, against only 4 deaths from asthma in the 449 patients first seen in childhood.

The "cures" are always interesting, and the group of mixed and unidentified cases whose asthma has ceased is particularly so. The 21 cases are shown in diagrammatic form in Figure 3. Seven patients (Nos. 1, 2, 11, 12, 13, 17 and 20) were relieved as soon as they moved away from home. Each of them showed a number of positive skin tests; their asthma was due to a sensitiveness to a dust substance of unknown nature but closely related to the home environment. When they were able to move away, the attacks ceased; the asthma was "cured."

Cases 5, 9, 18 and 19 are similar. When the kapok ("silk floss") in pillows and mattresses of poor quality was found and removed, the asthma cleared. Case 18 is interesting; the patient went to Arizona and was perfectly well there. In retrospect, one can say that the improvement depended not on any positive effect of the new climate but on a negative effect — escape from the kapok pillow that was causing trouble at home. She could have been relieved without the trouble and expense of a long journey.

Patient 4 lost his asthma at age nine, perhaps because of a simple change in the home environment. Recurrence came at age 19 when he spent the summer at a biological laboratory and was exposed to formalin. After age twenty-two, when he changed his job, he had no further asthma up to the follow-up at age forty-six. Treatment with vaccines was given to Patients 14, 16 and 21, and the results were good, perhaps because of the nonspecific effect. No obvious change in environment was made. Patient 15 is interesting; at age twenty-five his asthma cleared, and he gained weight. At age forty he developed a cough and wheeze. The symptoms persisted for about ten years, until finally his physician discovered gout and considered that the cough and wheeze were part of the picture, arising because of the "lowered resistance." On treatment by diet, atophan and vaccines, the man stopped wheezing at age fifty, and when last heard of he was hale and hearty at age 76.

Nasal polyps and sinusitis are more common in the older patients than in the younger group. All but 2 of the 15 patients with polypoid sinusitis had severe asthma and 1 died. Polypoid sinusitis carries a serious prognosis for cure of asthma, although only 12 out of 66 patients with asthma showed evidence of sinus difficulty, and these 12 were not necessarily all severe "sinus" cases. For example, in the animal-sensitivity group 1 patient had a cloudy antrum, another had an x-ray shadow, indicating ethmoid inflammation, and only 1 had definite polypoid sinusitis; he was greatly improved by treatment with ragweed and vaccine at age forty-three. Also, he had had an abscessed lower left incisor tooth removed. At age sixty-one he was not "cured," but he was much better. An occasional mild wheeze was easily controlled by adrenalin spray. There is no record of any nasal operation.

Two out of the 3 food-sensitive patients developed nasal polyps. The first was a baker, aged twenty-five, who had had a stuffy nose, with attacks of asthma, since age twelve. Skin tests showed large reactions to wheat, oats and rye. The rhinologist removed a large amount of polypoid tissue from both sides of the nose but did not touch the sinuses; the patient became more comfortable at that time. He changed his job and was treated with injections of wheat albumin, and wheat was excluded from his diet. Despite all this, his asthma, at age twenty-eight, was still severe. At age thirty-six, however, he was much better, except that his nose was still troublesome in spite of continued local treatment. One wonders whether this local treatment could have made the nasal symptoms worse, just as nose drops continued too long can make the nose stuffy as long as the drops are used.

The second patient, a woman of fifty-two with asthma in attacks since age twelve, had had nasal polyps removed a number of times between the ages of thirty-eight and fifty-two. On a wheat-free diet (skin tests were positive to wheat) she did very well. Treatment with vaccines seemed to help, and at age seventy-one she was comfortable — "getting good relief with Isuprel." None of the 5 polypoid-sinusitis cases noted under "Mixed and Unidentified" or the 2 under "Negative Tests" were severe. Two patients had had nasal operations, with no subsequent change in the frequency or severity of the asthma. In the past fifteen or twenty years the asthma continues in all of them but has not been severe in any. No one of this group of 66 patients has reported that his condition has been severe enough to require treatment in a hospital.

Twelve of these older patients have died — 6 probably of asthma. A man of twenty-three had had severe asthma all his life. Skin tests showed large positive reactions to animals and pollens. Specific treatment with horse and cat extracts and ragweed was of no avail. The man went to Arizona at age twenty-six; although he was able to marry and get along with epinephrine by needle and by nebulizer, his asthma never cleared. He died of cor pulmonale at age forty-four. The 2 patients in the mixed group died of asthma at ages forty-seven and fifty-two. The 3 patients with negative skin tests died at ages twenty-eight, forty-three and forty-eight, perhaps of asthma, as they all had severe cases with persistent, unrelenting symptoms that continued until the end.

Clearings of asthma with recurrences later occur in the older cases as in the younger group. Asthma depends on exposure to various dust substances. A boy went to college and was much better. He had no asthma from age nineteen to age thirty-one. In the Army Air Corps he was well until in India, at age thirty-one, he caught a bad cold; the asthma that followed was severe. It has continued up and down in troublesome fashion until the follow-up at age thirty-nine.

The elimination of the cat and the move from farm to city produce relief in the older as in the younger patients. It is not necessary to review the details. The fact that both relief and recurrence can come after age thirty is noteworthy; it makes all follow-up studies difficult and uncertain.

The later histories are similar to those in the first section of this report. The asthma improved, and

the patient, now in his forties or fifties, is well except for a seasonal hay fever, which is usually amenable to specific treatment. Again, it is interesting that the allergic substance to which sensitiveness is developed easily and in tenacious form is pollen.

Summary

Of 449 children with asthma seen before the age of thirteen, 138 cases, or 30.7 per cent, are entirely relieved of their symptoms. They appear to be "cured."

To state that asthma is "outgrown" at any certain age is not correct. The age of "cure" depends on the promptness with which the specific allergenic substances can be found and removed.

Another 19.5 per cent have no symptoms because they can successfully avoid the offending cause. They are still sensitive.

Still others (21.4 per cent of the whole) have no further asthma, but a new symptom, usually hay fever, has developed.

Nearly three quarters of the children have become cleared of asthma in their teens.

A fourth of all the patients are still in trouble, but this trouble is serious in less than an eighth (10.9 per cent) of the total.

Four of the 449 children died of asthma in their late twenties — a mortality of less than 1 per cent.

In the 449 children with asthma, boys outnumber girls about 2 to 1, and the proportion holds through all the classifications and through all the end results, including both successfully treated and refractory cases. Sex makes no difference in the outcome.

Asthma in children is due to allergy, sensitiveness to foreign substances in dust and occasionally (8 per cent) to foods.

In 18 per cent of the cases the history indicates trouble from head colds alone, and when the skin tests in these cases are negative the diagnosis of "bacterial asthma" seems indicated even though it is hard to prove. The term "bacterial allergy" may define the mechanism.

"Asthmatic bronchitis" is a useful term that indicates that new head colds lower the threshold to make a slight allergy effective. When head colds produce a wheeze, the patient is sensitive to some dust in his environment, but if he does not wheeze with his colds one can assume that he is no longer in contact with the offending substance — or else that his former sensitiveness has cleared.

The changes in the direction of sensitiveness are interesting. The typical sequence is: eczema in infancy due to foods, especially to egg and cow's milk; asthma in childhood from dusts, especially animal danders; and later hay fever from pollen. The basic lesion is not the allergy; it is the capacity to develop sensitiveness.

"Cures," or clearances of the asthma, may seem complete, but all too often some new manifestation develops after a period of years.

That this new episode is hay fever in most of the cases indicates some peculiar quality (chemistry) of pollen to make it an excellent allergen (sensitiveness is acquired easily) but a poor antigen (antibodies develop slowly, if at all).

Sometimes asthma will recur after a free period of ten to fifteen years. In 2 out of 6 cases this recurrence was due to allergy — to pollen. In the others, only the fact of recurrence is known.

A review of older patients, — not seen until after their childhood, — shows that changes in the progress of the disease may occur at any age. Follow-up studies must be continued for a long time.

Polypoid paranasal sinusitis is rare in children with asthma. In the older group, however, it was seen in 15 of the 239 cases. It was found more often in severe cases than in mild ones.

The relation between the older patients who first had asthma in childhood and the other older patients who developed their asthma for the first time after age forty, to which the term "intrinsic" has been applied, — meaning that the exciting cause is inside the body and not allergy at all, — remains a problem for future study.

MEDICAL INTELLIGENCE

THE ROUTINE GUAIAC STOOL TEST

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AN EVALUATION of the importance of routine stool testing in the internist's office for occult blood was made by reviewing 1600 consecutive office records of new patients.

Stool specimens brought to the office in a container proved more satisfactory than those obtained on the gloved finger at routine rectal examination. A light-green discoloration of the stool and chemical mixture on a white porcelain-tile plate was graded as + and was considered of no importance. A bluish-green color developing slowly (over a period of more than one minute) was graded as ++ and was classed as equivocal. A definitely blue reaction, developing slowly, was graded as +++. The immediate development of a deep-blue color was classed as ++++. Patients showing positive tests were instructed to send another specimen. Investigation of the gastrointestinal tract by x-ray and the sigmoidoscope was recommended in most cases if subsequent tests were also positive.

Seventy-seven of 1600 patients studied showed positive guaiac tests on the first specimen. Thirty-seven of this group were not studied further because of a negative reaction of subsequent specimens or because they could not be followed, for various reasons. Patients showing initially positive tests and subsequent negative tests present a challenge. A conclusion that no disease exists because subsequent tests were negative may admittedly be a fallacious one. A patient whose first two tests were strongly positive was proved to have carcinoma of the hepatic flexure, although a number of subsequent tests were negative. The need for a simple, realistic application of the test, however, suggested that minimal follow-up study was indicated in those patients showing initially positive but subsequently negative reactions.

Forty patients showed two consecutively positive tests and were investigated further. Four of these were not clinically suspected as having gastrointestinal disease. The positive test initiated studies that led to the discovery of carcinoma of the sigmoid in one patient, of an ulcer crater in the duodenum of another patient (whose ulcer was clinically silent) and of multiple polyps of the sigmoid in two others. The test was considered "substantiative" in 27 patients. A clinical suspicion of gastrointestinal disease was entertained in these cases. Further investigation proved the suspicion to be well founded.

Persistently positive reactions in 3 patients suspected of large-bowel cancer led to the discovery of carcinomas at surgical exploration, despite normal barium-enema examinations. An inability to demonstrate a hepatic-flexure carcinoma on two separate fluoroscopic and x-ray trials resulted from the roentgenologist's failure to turn the patient properly from side to side. The guaiac test was more dependable than the roentgenologic examination in these 3 cases.

Nine patients showed no clinical evidence of disease, by x-ray or the sigmoidoscope, although +++ or ++++ reactions were obtained. Upper gastrointestinal series were not routinely carried out in this group unless some gastric symptom or complaint was present. Although "silent" lesions may occur in the stomach and duodenum, they are more numerous in the large bowel. Because of this, the upper-gastrointestinal series was omitted when the expense of such an examination would have been too burdensome.

Two patients having negative guaiac tests were suspected clinically of having disease. Surgical exploration proved carcinoma of the stomach in one patient whose upper-gastrointestinal series was positive. X-ray examination of a second patient showed an active perforating duodenal ulcer. Sigmoidoscopic examination of the same patient revealed multiple polyps of the sigmoid.

On the basis of the present study, the value of the guaiac test for occult blood in the stool as a screening test seems established, in spite of the contention of one author[1] that the test "was discarded twenty-five years ago." The recommendation, by this same author, of spectroscopic examination of the specimen is difficult to reconcile with a practical, logical approach. The pitfalls of error of the sensitive benzidine test[2] are well established. An increase in the sensitivity of testing can lead only to increased error. In spite of the lack of specificity and the margin of error of the guaiac test, it has demonstrated its value in a reasonable number of cases in the present study.

SUMMARY AND CONCLUSIONS

Guaiac tests were made on the stool specimens of 1600 consecutive new office patients.

Seventy-seven patients were found to have a positive reaction on the first specimen.

Forty patients had positive reactions on subsequent specimens and were studied by x-ray and sigmoidoscopy. The test was diagnostic in 4 of this group, since disease was not clinically suspected,

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and substantiative in 27 patients who were considered on clinical grounds to have disease. The test was misleading in 9 patients who showed no evidence of gastrointestinal disease on roentgenologic, sigmoidoscopic or clinical evaluation.

Repeatedly positive tests of 3 patients suspected of large-bowel cancer led to definitive investigation in spite of negative barium-enema examinations. Carcinoma of the bowel was found at operation in each case.

Negative tests were demonstrated in a patient with extensive carcinoma of the stomach and in a patient with an acute perforating duodenal ulcer and polyposis of the sigmoid.

TABLE 1. *Value of Guaiac Stool Test in 43 Cases.*

PATIENT	VALUE OF GUAIAC STOOL TEST	FINDINGS AT UPPER-GASTROINTESTINAL EXAMINATION	FINDINGS AT BARIUM-ENEMA EXAMINATION	FINDINGS AT SIGMOIDOSCOPY	CLINICAL DIAGNOSIS
R. B.	Diagnostic	Duodenal ulcer	Normal	Normal	No disease
S. A.	Diagnostic	Normal	Normal	Multiple polyps	
L. B.	Diagnostic	Normal	Polyps of sigmoid	Multiple polyps	
R. R.	Diagnostic		Carcinoma of sigmoid proved at surgery	Partial obstruction at 15 cm.	Rheumatoid arthritis
J. A.	Substantiative	Prepyloric ulcer	Normal	Normal	Peptic ulcer
P. A.	Substantiative	Duodenal ulcer			Peptic ulcer
D. B.	Substantiative		Normal	Granular mucous membrane; single small polyp	Mucous colitis
E. B.	Substantiative				Past history of duodenal ulcer; recent tarry stools
F. B.	Substantiative				Past history of duodenal ulcer
M. B.	Substantiative		Diverticulosis of sigmoid	Areas of edema, irritation, healed ulcers	Spastic bowel and diverticulitis
L. B.	Substantiative		Two negative examinations; Trial 3 showed lesion at hepatic flexure; carcinoma found at operation	Normal	Carcinoma of bowel
P. B.	Substantiative		Normal	Normal	Fissure in ano; hemorrhoids
T. B.	Substantiative		Normal	Superficial plexus of veins	Mucous colitis
M. C.	Substantiative		Diverticulosis and diverticulitis	Normal	Spastic bowel
M. G.	Substantiative		Carcinoma of bowel removed 1 yr. previously; present x-ray film negative for recurrence		Recurrence of carcinoma proved by surgery
C. G.	Substantiative	Duodenal ulcer	Diverticulosis and diverticulitis	Healed granulations and "pock" marks	Peptic ulcer and spastic bowel
M. H.	Substantiative		Original x-ray film normal; carcinoma of sigmoid in subsequent examination		Carcinoma of bowel proved at surgery
M. H.	Substantiative			Ulcerative colitis	Ulcerative colitis
B. K.	Substantiative		Normal	Normal	Mucous colitis
A. L.	Substantiative	Normal	Normal	Normal	Irritable bowel
F. L.	Substantiative		Diverticulosis and diverticulitis		Diverticulitis
G. M.	Substantiative				Spastic bowel with mucous colitis
G. M.	Substantiative				Spastic bowel with mucous colitis
P. G.	Substantiative				Spastic bowel with mucous colitis
V. C.	Substantiative				Spastic bowel with mucous colitis
M. N.	Substantiative		Diverticulosis and diverticulitis		Irritable bowel with mucous colitis
J. R.	Substantiative		Loss of haustral markings with straightening	Reddened, edematous mucous membrane	Allergic colitis
J. S.	Substantiative	Duodenal ulcer			Peptic ulcer
S. S.	Substantiative		Normal	++ mucus and irritability	Spastic bowel
A. T.	Substantiative	Duodenal ulcer	Normal	Normal	Peptic ulcer; spastic bowel
J. V.	Substantiative	Duodenal ulcer			Peptic ulcer
A. W.	Substantiative	Duodenal ulcer	Normal	Normal	Peptic ulcer; spastic bowel
J. F.	Misleading negative guaiac test	Carcinoma of stomach			Functional gastric disease
T. M.	Misleading negative guaiac test	Duodenal ulcer	Normal	Multiple polyps	Functional gastric disease; spastic bowel
M. B.	Guaiac positive; no disease found		Normal	Normal	
P. B.	Guaiac positive; no disease found		Normal	Normal	
T. C.	Guaiac positive; no disease found		Normal	Normal	
A. H.	Guaiac positive; no disease found	Normal	Normal	Normal	
R. K.	Guaiac positive; no disease found	Normal	Normal	Normal	
H. Mc.	Guaiac positive; no disease found	Normal	Normal	Normal	
H. N.	Guaiac positive; no disease found	Normal	Normal	Normal	
L. R.	Guaiac positive; no disease found	Normal	Normal	Normal	
C. Y.	Guaiac positive; no disease found	Normal	Normal	Normal	

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The study reveals a suggestive margin of error of 11 of 1600 tests. Nine of these were falsely positive and hence of no detriment to the patient. In only 2 recognized cases did the test fail to demonstrate existing disease.

Addendum

Since this paper was written, the guaiac test has been "diagnostic" in two more cases. Positive tests in an adult man complaining of back and shoulder pain, with no gastrointestinal symptoms, led to the discovery of an extensive inoperable carcinoma of the stomach. Repeatedly positive tests in a woman who had a recent "normal" barium-enema examination led to further roentgenologic investigation, which demonstrated a carcinoma of the sigmoid, later proved at surgery. Review of the original barium-enema films revealed on close inspection that the lesion was present at that time.

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DOCTORS AFIELD

Inspired partly by the interesting story of Jan Van Riebeeck, the doctor who settled Cape Town, contributed by Dr. Viets to Medical Intelligence in the issue of March 27 and partly, perhaps, by the weather, the editors of the *Journal*, accustomed as they are to great responsibilities, have assumed a new one. It is to publish from time to time, as space and material may be available, brief accounts of physicians who have achieved a degree of success or even fame in some activity other than the pursuit of medicine in its various branches.

The very particular editor of this particular series will welcome both suggestions and contributions, which will be used according to their merit.

Dr. Archagathos: Refugee Physician and Roman Consul

Robert W. Buck, M.D.
Boston

THE physician Archagathos, who emigrated from Greece to Italy in 219 B.C., is supposed to have been the first man to practice medicine in Rome.[1] He soon gained wide popularity as a healer of wounds and was showered with honors, including Roman citizenship. He thus became, it is said,[2-4] the founder of the Acilian gens, one of the better known plebeian families. Eventually, because of his free use of scalpel and cautery, he attained a reputation as a butcher and apparently gave up his practice. He seems to have incurred the particular displeasure of Cato the Elder, but this did not prevent his subsequent rise to political prominence.

In 201 B.C., as Manius Acilius Glabrio, tribune of the plebs or trial representative (an office not unlike that of the contemporary city councilor or member of the state legislature), he successfully obstructed the claim of Consul Cn. Cornelius Lentulus to the province of Africa, previously awarded by popular vote to Scipio; in the following year he was appointed commissioner of sacred rites. In 196 B.C. he was made a subconsular magistrate, and in 197 he put down an insurrection of serfs in Etruria. Four years later he ran, unsuccessfully, for the consulship, but was elected to that office in 191. It was in this year that he achieved his greatest claim to fame, for as consul he was sent back to Greece at the head of an expeditionary force to carry out a police action against the Syrian aggressor Antiochus the Great. Glabrio finally defeated Antiochus at Thermopylae and the following year was unanimously granted a magnificent triumph, although, like General MacArthur, he had to enjoy it without his troops, who remained in Greece under the command of his successor, L. Cornelius Scipio. In 189 B.C. he was a popular candidate for the censorship, but his old enemies, the nobles, objected to him as an upstart, and his rival M. Cato accused him of privately sequestering some of the royal loot obtained from Antiochus. Glabrio withdrew from the contest, accusing Cato of perjury.

Eight years later, when, if still alive, he was an aging man, his son dedicated in his name a temple of Pietas in the Forum Olitorium and in it set up a gold-plated statue of his father — the first of its kind seen in Italy.[5, 6]

The Acilii Glabriones reappear from time to time throughout the history of the Republic and the Empire. In about 50 B.C. a descendant, Manius Acilius Glabrio, one of Julius Caesar's lieutenants and triumvir of the mint, issued a silver denarius that, according to Mommsen,[4] commemorates the family claim to descent from Archagathos.

The coin (Fig. 1) bears a representation of Salus, goddess of health, and the reverse portrays Valetudo holding a serpent (emblem of health and longevity), with the circumscription MN. ACILIVS III. VIR. VALETV. (Manius Acilius, triumvir, Valetudinis).

Figure 1.

In 95 A.D. a later Mn. Acilius Glabrio was put to death by Domitian on the charge of "having drifted into Jewish ways" and, in particular, of fighting as a gladiator with wild beasts.[7]

Why did Dr. Archagathos change his name? Probably for social reasons. Mommsen[8] suggests that the family name Acilius derives from the Greek root ἀκή (healing) in reference to the profession of its ancestor. He was probably bald — hence Glabrio, since the cognomen commonly referred to some personal peculiarity of the individual, as Cicero (warty), Brutus (stupid) or Pansa (flat footed). Manius was his given name. Since Plinius is referred to as Pliny, Livius as Livy and Tullius as Tully, Manius might be called Manny. *Archagathos* means "a good (or very good) man."

It is not, then, too far fetched a conclusion if we surmise that Dr. Manny Goodman (Manius Archagathos), fleeing the wars in Greece, escaped to Rome, where he settled as a refugee physician and established a successful practice, much to the disgust of the conservative Roman families such as the Catos. He became a Roman citizen, Latinized his name from Goodman to Bald Healer (Acilius Glabrio), probably married an Italian girl and after giving up his waning practice went into politics, becoming the prototype of all physicians who have demonstrated that fame is an accident rather than the result of a man's education or profession.

5 Bay State Road

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8. Mommsen,[4] ii: 498.[5] Note 1.

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 38221

PRESENTATION OF CASE

First admission. A forty-one-year-old man was admitted to the hospital because of dyspnea and severe low-back pain.

Five years prior to entry the patient noted that the distal end of the fingers and toes were enlarging progressively. Shortly after this he developed a chronic nonproductive cough that was most severe in the morning and that progressed slowly in severity; about six months prior to admission it became productive of small amounts of mucoid sputum. In addition the patient noted that he became short of breath on exertion. Four months before admission intermittent low-back pain appeared and gradually increased in frequency and severity until it was finally constantly present; there was no radiation of the pain; it was unaffected by posture, straining and sneezing and was not relieved by aspirin. Two months prior to entry the cough became much more severe; he had severe malaise, and when he smoked he developed a pain in the left chest. His physician told him he had "a touch of pneumonia" and treated him with pills; after two days he developed a rash in the puboinguinal region and had to discontinue these. Slow progression of all the symptoms continued. His exercise tolerance became limited to climbing one flight of stairs or walking half a block on the level ground, after which he would have fairly marked dyspnea; he found he was able to breathe most easily when he was lying flat in bed. He was anorexic, had become progressively weaker and had lost 10 pounds in weight in the month before entry. He had had night sweats for many years. There had been no chills or hemoptysis.

The patient had been exposed to heavy concentrations of dust in an asbestos mill for twelve years; he had stopped working there two years before admission. Although he had worn a mask he stated that "usually there was more dust on the inside than the outside." He had used one can of snuff and smoked one to two packs of cigarettes daily for many years.

Physical examination revealed a poorly nourished man who was mildly dyspneic while lying in bed and who seemed to be in considerable distress. There was questionable mild cyanosis of the lips and fingers and marked clubbing of the fingers and toes. The neck veins were flat. There was poor respiratory expansion and the thorax was rigid and thin. Both lung bases were relatively dull to percussion, and in addition on the right there was increased tactile fremitus, diminished breath sounds and a number of loud sticky rales. The heart appeared to be slightly enlarged. The pulmonary second sound was greater than the aortic, and there were frequent extrasystoles. The liver edge was palpable 1 cm. below the costal margin. The prostate was slightly tender but was not enlarged or nodular. There was no localized tenderness over the spine or sacrum. There was spasm of the lumbar muscles with marked

limitation of back motion; lateral flexion caused considerable pain and straight leg raising was limited bilaterally, more so on the left. The lower extremities were not remarkable.

The temperature was 98°F., the pulse 90 and the respirations 18. The blood pressure was 110 systolic, 75 diastolic.

A urine of specific gravity 1.018 was normal. Examination of the blood showed a hemoglobin of 14 gm. and a white-cell count of 5700, with a normal differential. An erythrocyte sedimentation rate was 0.45 mm. per minute. The total protein was 6.88 gm., the albumin 4.06 gm., the globulin 2.82 gm., the nonprotein nitrogen 27 mg., the fasting blood sugar 98 mg., the serum calcium 9.5 mg., the phosphorus 3.7 mg., the alkaline phosphatase 4.9 units and the acid phosphatase 1.6 units per 100 cc. The serum sodium was 139.1 milliequiv., the chloride 100 milliequiv., the potassium 4.6 milliequiv.

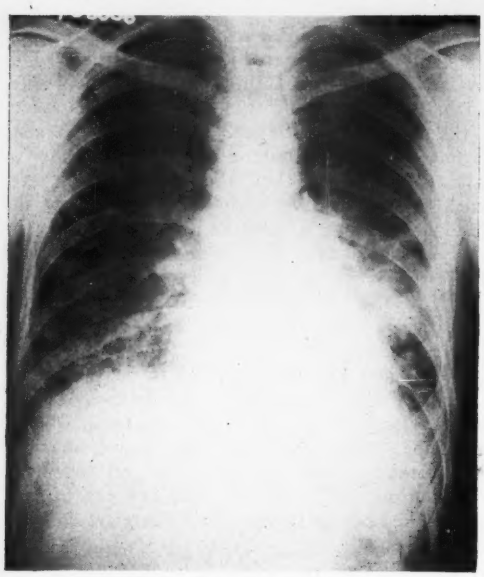

FIGURE 1.

and the carbon dioxide 29.4 milliequiv. per liter. A guaiac test of the stool was negative. Roentgenograms of the chest revealed each lower lobe to be reduced in size, with a honeycomb pattern at each base (Fig. 1). There was a poorly defined area of homogeneous density in the lingula. The lung roots appeared enlarged and on the left there was a suggestion of lymph-node enlargement with calcification. The left ventricle was somewhat rounded and the left costophrenic angle was blunted. Laminograms showed an area of narrowing in the left main bronchus; no nodal enlargement could be demonstrated. Fluoroscopy showed a fixed left diaphragm. Roentgenograms of the spine showed areas of decreased and areas of increased density in the body of the fourth lumbar vertebra (Fig. 2).

X-ray films of the skull were negative. X-ray films of the extremities showed periosteal new-bone formation about the distal ends of peripheral long bones. At bronchoscopy the left-lower-lobe bronchus was narrowed by a lesion that was friable and bled easily; biopsy of this area showed small fragments of keratinized epithelium. Smears of the bronchial

FIGURE 2.

washings and sputum were negative for acid-fast organisms and for birefringent bodies; cytologic smears were reported as "doubtful for malignant cells" on two specimens and negative on numerous others. Cultures of the sputum yielded abundant alpha hemolytic streptococci and Monilia. An electrocardiogram showed nonspecific T-wave changes. A bone-marrow smear showed a normal marrow with eosinophilic predominance. A tuberculin test (1:10,000 dilution) was negative.

Intramuscular penicillin therapy had little effect on the condition. It was next decided to see whether ACTH (adrenocorticotrophic hormone) therapy would benefit him and he was given 100 mg. a day for ten days. A satisfactory response as judged by the eosinophil count was obtained. Pre- and post-therapy pulmonary function and cardiac catheterization studies were carried out. Before therapy pulmonary function studies showed the following: the vital capacity was 2.4 liters as against a predicted vital capacity of 3.9; the maximum breathing capacity was 50 per cent of the expected value; the alveolar-arterial oxygen difference equaled 27 mm. of mercury. Post-therapy studies showed no significant changes. Pre-therapy cardiac catheterization studies revealed the following: at rest, the blood pressure in the pulmonary artery was 36 systolic, 14 diastolic, the radial-artery oxygen saturation 94 per cent and the cardiac output 7.1

liters per minute; after exercise the pulmonary-artery pressure rose to 43 systolic, 14 diastolic, the radial-artery oxygen saturation fell to 89 per cent and the cardiac output increased to 8.8 liters per minute. The right-auricular pressure was equivalent to ±0 mm. of mercury. Post-therapy cardiac catheterization studies showed no significant change in these values.

While on ACTH therapy the patient became quite euphoric and claimed to be able to breathe more easily, but objectively there was no change in his condition. After the drug was discontinued he became quite depressed and complained of increasing dyspnea, generalized aches and a return of the back pain. Roentgenograms of the chest after five weeks of hospitalization showed no appreciable change, but x-ray films of the lumbar spine showed additional bone destruction of the body of the fourth lumbar vertebra. X-ray therapy (1200 r) was given to the fourth lumbar vertebra; roentgenograms of the spine taken after the completion of this demonstrated no change. He was discharged relatively unchanged after two months in the hospital; the back pain was somewhat less severe and was easily controlled with aspirin or codeine.

Second admission (two months later). In the interval the dyspnea had been very severe for the first six weeks but then it definitely improved; the patient felt much better and returned to light work. The cough and lumbar pain had persisted. During the four days before admission the dyspnea became markedly increased to the point that he could hardly take any steps and could hardly talk. He was also wheezing a great deal. There had been no chills or fever, chest pain or hemoptysis.

Physical examination revealed a thin, sallow man who was so dyspneic at rest that he found it difficult to talk. The neck veins were full. There were bubbling rales throughout both lungs, tachycardia, slight hepatomegaly and + to ++ ankle edema. Otherwise the findings were similar to the first admission.

The temperature was 101°F., the pulse 120 and the respirations 40. The blood pressure was 120 systolic, 80 diastolic.

Examination of the blood revealed a hemoglobin of 11.5 gm. and a white-cell count of 6500 with 88 per cent neutrophils. Urinalysis and blood cultures were negative. Cultures of the sputum grew alpha hemolytic streptococci and a few *Staphylococcus albus*.

Roentgenograms of the chest showed a marked increase in the linear and nodular markings throughout the chest (Fig. 3).

He was treated with Mercuhydrin, antibiotics, antispasmodics, digitalis and continuous oxygen therapy. There was some temporary improvement, but he continued to have marked dyspnea and violent spasms of coughing. He died on the thirty-fourth day.

Differential Diagnosis

Dr. W. Melville Arnott*: May I first thank you for the opportunity of taking an active part in this Cabot Case Conference, the original, the prototype of all clinical pathological conferences.

Here are the x-ray films that have been given me, and I shall ask the radiologist if he will be kind enough to interpret them.

Dr. Joseph Hanelin: The chest films extend over a four-month period before the patient's death (Fig. 1 and 3). As indicated in the protocol, there is extensive disease in the lungs, mostly in the lower lobes, and a fair amount of pleural reaction at the left base. In an over-penetrated film it is possible to visualize abrupt termination of the left lower bronchus shortly after its origin. About two months after the first films were made, there is evidence of further involvement of both lungs, now affecting all the lobes, and to about the same degree on either side, although in the initial films involvement preponderates on the left. The fourth lumbar body is involved by a process that seems to be both osteolytic and osteoblastic (Fig. 2). It has not resulted in any particular collapse of the vertebra, but there does seem to be a very definite destructive change. There is also a suggestion of a somewhat similar lesion that involves the medial aspect of the right iliac wing. Over the period of observation of the vertebral lesion there was evidence of rather slowly progressive destruction.

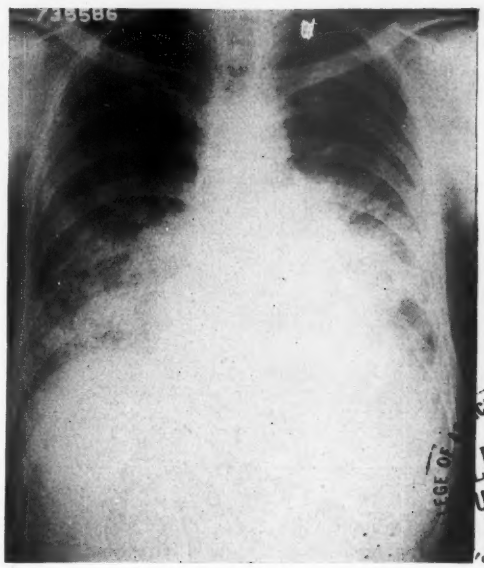

Figure 3.

Dr. Arnott: The clinical history shows that the progress of events was in two phases: the first, four

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and a half years before admission, commencing at the age of thirty-six, was marked only by clubbing of the fingers and toes and cough, but without noticeable dyspnea; during the last six months of life there developed increased dyspnea, mucoid sputum, loss of weight and pain in the left side of the chest, while in the terminal few weeks there was evidence of congestive failure with fever. There is a history that from the age of twenty-seven to thirty-nine he had worked in an asbestos mill, where he claimed to have been in an extremely dusty atmosphere.

The physiologic studies I shall deal with first. I have been given more data obtained from the observations carried out on the patient by Dr. B. C. Ferris, and these points, as well as the salient data given in the history, I have summarized here (Table 1). The maximum breathing capacity was reduced to about 50 per cent of normal. His vital capacity was reduced. His residual air was relatively unchanged and the ratio of vital capacity to total capacity was not very abnormal. The main defect

TABLE 1.

	ACTUAL VALUE	CALCULATED NORMAL VALUE FOR THIS PATIENT
Maximum breathing capacity	50%	100%
Vital capacity	2.4 liters	3.9 liters
Residual air	1.49 liters	1.6 liters
Total lung capacity	3.89 liters	5.5 liters
Ratio of residual air to total lung capacity	0.38	0.32
Alveolar pO_2	115 mm.	107 mm.
Arterial pO_2	88 mm.	95 mm.
Arterial pCO_2	36 mm.	39 mm.
Alveolar-arterial O_2 difference	27 mm.	12 mm.
Effective alveolar ventilation	6 liters per min. per sq. meter of body surface	2.2 liters per min. per sq. meter of body surface

in lung volume, then, was a reduction of vital capacity, and it seemed to be a reduction in the inspiratory reserve volume, or the complemental air, as it used to be called. The alveolar oxygen — 115 mm. of mercury — was rather above the normal. On exercise the arterial blood oxygen was 88, and the alveolo-capillary oxygen difference was 27 mm. compared with a normal of 12 — a figure that indicates a diffusion defect. Further evidence that the defect is one of diffusion and not of alveolar ventilation is the pCO_2, which in the blood was only 36 mm., a low figure, whereas with a serious defect in alveolar ventilation the carbon-dioxide tension is invariably increased. From the physiologic standpoint, an alveolo-capillary diffusion defect, therefore, is established beyond any shadow of doubt.

The cardiac-catheterization studies show that there was a slight elevation of both systolic and diastolic pressures. In the only study carried out, before the final phase of the congestive failure, the right auricular pressure was normal; no doubt in the closing weeks it rose in conformity with the cardiac failure. On exercise it rose even further, whereas in a normal person on exercise the pulmonary arterial pressures do not rise or may even fall. The effective alveolar ventilation was calculated, and the figure was 6 liters per minute per sq. meter of body surface opposed to a normal of 2.2. This hyperventilation raised alveolar-oxygen tension, thus raising the alveolo-capillary O_2 quotient — an adaptation to the diffusion difficulty presented by thickened capillary walls.

The next step in the elucidation of the case is what disease process would conform to the clinical features and the known physiologic defects. There were two nonrespiratory factors dominating the data; these were the back pain and the changes in the lumbar vertebra, which seem to be impossible to explain on any basis other than that of neoplasm. A likely sequence of events is that he had a carcinoma of the lower lobe of the left lung that had caused metastatic deposits in the vertebral column. However, the history extended back five years and there were the diffuse changes in the lower fields of both lungs. The pleural reaction and the fuzzy "porcupine-like" appearance of the heart are changes that are known to occur in berylliosis and I believe also in asbestosis, although I have never seen a case of asbestosis. I think it is quite a reasonable assumption, although there was nothing found to prove conclusively that the patient had asbestosis and that the terminal illness was due to superimposed carcinoma of the lung with metastatic deposits. There is a belief that silicosis and asbestosis predispose to carcinoma of the lung, a belief that is, as far as I know, based not on statistical evidence but rather on isolated case records.

What are the other differential diagnoses? In a case like this one has always to think of tuberculosis. Against tuberculosis are the x-ray appearance, which is quite unlike tuberculosis, the sputum that was repeatedly negative, the material removed from the friable lesion in the left-lower-lobe bronchus negative for acid-fast bacilli and the negative tuberculin test; all those taken together make the diagnosis of tuberculosis extremely unlikely. Tuberculosis was obviously also considered unlikely by those who cared for the patient; otherwise they would not have given ACTH and would not ultimately have used deep x-ray therapy on the lesion of the vertebral column. One other possibility that occurred to me is coccidioidomycosis, which, I understand, can cause lesions in the lungs and the bones and might possibly produce a picture not unlike this. I am speaking theoretically, as I have never seen a case of coccidioidomycosis; I understand it occurs only in the southwestern part of North America and its development in a native of the northeast would be quite exceptional. The points against it are the long history, the absence of cavitations in the lungs, no eosinophilia and the bone changes, which, so far as I know, are quite unlike those of coccidioidomycosis. Furthermore,

fever was not a prominent feature of this case and there were no skin changes.

Pulmonary sarcoidosis is only a remote possibility.

In conclusion my prediction is that the patient had asbestosis, complicated by carcinoma of the lung and cor pulmonale. There is a great tendency to ascribe disease like carcinoma of the lung to asbestosis, yet I do not believe the number of cases of carcinoma of the lung in asbestosis is great enough.

DR. ALBERT O. SEELER: I have no comments except to mention a recent case report[1] in which a large series of cases of asbestosis and malignant disease in the lung that had appeared in the literature were reviewed; there was a higher incidence of malignant disease in asbestosis than one would expect to see in pulmonary disease in general.

DR. JOSEPH C. AUB: The man smoked between 20 to 30 cigarettes a day and took snuff besides.

DR. WALTER BAUER: Would it disturb you to make a diagnosis of asbestosis despite the fact that the disease was confined to the lower lobes?

DR. ARNOTT: From the literature I understood that the pathologic changes are much more marked in the lower lobes.

DR. EDWARD B. BENEDICT: I believe there is good evidence in the literature that carcinoma of the lung has a higher incidence in asbestosis.

DR. BENJAMIN CASTLEMAN: According to the papers that have been written in the last five years, between 10 and 15 per cent of people with asbestosis develop carcinoma. That is the figure that is given in the paper Dr. Seeler referred to, and there have been several others; particularly in a review of cases in the New Haven Hospital,[2] the incidence of carcinoma was very high.

Dr. Ropes, you saw this patient; would you tell us the opinion on the ward?

DR. MARIAN ROPES: Our reasoning was very much the same; we thought that the picture was typical of asbestosis after we learned about asbestosis; we assumed, largely because of the back lesion, that there was also a malignancy in the lung, with metastases. Although we were unable to get any support from study of the cells in the sputum or from a trocar biopsy of the vertebra, a malignant lesion superimposed on the asbestosis still remained as the likely possibility. The ACTH was given both to study the physiologic reaction in this condition and to compare it with the reaction in the berylliosis.

CLINICAL DIAGNOSES

Asbestosis.
Carcinoma of lung with metastasis to fourth lumbar vertebra.

DR. ARNOTT'S DIAGNOSES

Asbestosis.
Carcinoma of the lung with metastases.
Cor pulmonale.

ANATOMICAL DIAGNOSES

Pulmonary asbestosis.
Adenocarcinoma of the lung with invasion of heart and with metastases to bronchial lymph nodes and fourth lumbar vertebra.
Cor pulmonale.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: The lungs were voluminous and very heavy and contained little air. There was marked thickening of the pleura with obliteration of all septa on both sides and with very marked interadherence between the pleura and parietal pericardium. This pleuritis is quite the rule in asbestosis. Section showed extreme fibrosis throughout most of the lung, even in the upper lobe. Microscopically, alveolar epithelialization, which occurs with many chronic pneumonitic processes, was very prominent. The striking finding was the myriads of asbestos bodies, many of which were covered with hemosiderin and stained brown in the ordinary hematoxylin-and-eosin stain (Fig. 4). The asbestos bodies were primarily in the larger bronchioles and extended down as far as the respiratory bronchiole and occasionally into an alveolus. These bodies are so large that they usually cannot go beyond the size of the respiratory bronchioles. Marked thickening of the intima with luminal narrowing of all the arteries throughout the lung was good evidence of hypertension in the pulmonary circuit and this, as expected, was associated with hypertrophy of the right ventricular wall, which was about twice the

FIGURE 4.

normal thickness — a true cor pulmonale. A quite prominent feature was the marked squamous-cell metaplasia of bronchioles throughout the lung. The chronic process had apparently stimulated this squamous-cell metaplasia, which may be the precursor to the development of a carcinoma, and if so, one would expect a squamous-cell carcinoma. The left-lower-lobe bronchus was occluded by a carcinoma, which extended into the lung parenchyma medially to the pleura to invade the left auricular wall (Fig. 5), but microscopical examination showed it to be an adenocarcinoma. The fourth lumbar vertebra contained adenocarcinoma similar to that in the lung, and there were also metastases to a few of the regional lymph nodes.

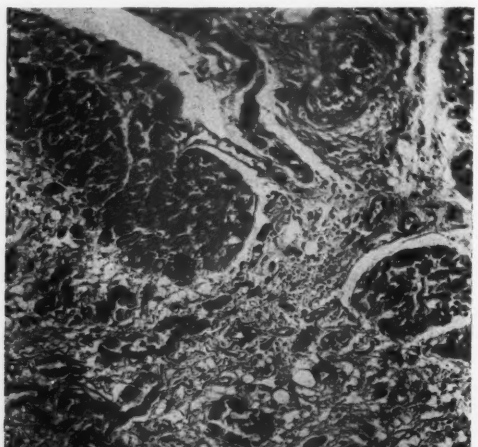

FIGURE 5.

DR. J. H. MEANS: What is being done to prevent this disease? Were the protective devices inadequate, or was there any other neglect here in protecting these persons? Where was this man working?

DR. ROPES: Dr. Harriet Hardy investigated this. It was a very poorly run mill from the point of view of protection of the worker, and unfortunately even from the point of view of insurance this man was not covered because the legal time interval had elapsed between the patient's leaving work and complaining of symptoms. The State has checked up on the mill now.

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CASE 38222

PRESENTATION OF CASE

First admission. A sixty-one-year-old man was admitted to the hospital because of severe pressing substernal pain.

Three hours prior to entry, while riding in an automobile, the patient suddenly developed a severe pressing substernal pain that radiated to the left arm and was unrelenting. He rapidly became pale and sweaty, felt nauseated and vomited once.

The patient had never experienced chest pain in the past and had been free of cardiac symptoms. For years he had been troubled with epigastric pain, which usually began several hours after a meal or if he missed a meal, and which was relieved by milk and baking soda. A gastrointestinal series several years prior to entry was negative.

Physical examination disclosed a pale, cold, sweaty man complaining of severe chest pain. The neck veins were flat. Fine crepitant rales were heard in both lungs posteriorly up to the level of the ninth thoracic vertebra. The heart and abdomen were normal.

The temperature was 97.0°F., the pulse 80 and the blood pressure 110 systolic, 74 diastolic. Respirations were of the Cheyne–Stokes type.

The urine, of specific gravity 1.018, was normal. The white-cell count was 14,000, with 67 per cent neutrophils, and the hemoglobin was 15.0 gm. The nonprotein nitrogen was 53 mg. per 100 cc. An electrocardiogram showed normal rhythm at a rate of 70 with occasional ventricular premature beats, a PR interval of 0.17 second, a QRS interval of 0.14 second and normal voltage. There were Q waves present in Leads AVL, V_1, V_2 and V_3. The ST segment was elevated in Leads AVR, AVL, V_1, V_2, V_3 and V_4.

The patient was treated initially with morphine and oxygen; quinidine, digitalis and Dicumarol were added to the regimen soon afterwards. He made a slow uneventful recovery and was discharged on the thirty-third hospital day on a daily dose of digitoxin.

Final admission (fifteen months later). In the interval the patient had been followed periodically in the Medical Clinic. Except for some pain in the left arm, he was free of cardiac symptoms. One year prior to entry he began to complain of recurrence of the postprandial epigastric pain, which

radiated through to the back and which was relieved by milk and baking soda. The pain frequently awakened him during the night. He was started on a six-meal bland diet and given antacids and tincture of belladonna. Ten months prior to entry he vomited or coughed up about a teaspoonful of bright-red blood and was admitted to the Emergency Ward. Examination revealed moderate epigastric tenderness on deep palpation, and 400 cc. of guaiac-negative milky fluid was aspirated from the stomach. Roentgenographic examination done the following day showed retention of gastric fluid, coarsening of the gastric mucosal pattern and marked deformity of the duodenal cap. No ulcer crater was demonstrated. Chest films revealed enlargement of the heart, tortuosity and sclerosis of the aorta and some increased linear densities extending into the posterior basal segment of the right lower lobe. He was discharged from the Emergency Ward the following day on the same ulcer regimen. During the next six months he improved considerably and at the end of that time discontinued all medications. Three days before entry, he had the sudden return of epigastric pain and took only liquids by mouth. He shortly thereafter began to vomit and continued to do so up to the time of admission. Eighteen hours before entry his midepigastric pain became more severe. Two "injections" by his local physician failed to relieve the pain. He spent a restless night and was cold and sweaty. Seven hours before entry he lost consciousness for a few minutes, was incontinent of urine and on regaining consciousness "could not talk right." Two hours before entry he had a generalized convulsion lasting a few seconds, followed immediately by drooping of the right side of the face. He did not recover consciousness.

On physical examination, he was comatose and deeply cyanotic, with stertorous respirations. The head and eyes were turned to the right. The pupils were small and did not react to light. The corneal reflex was absent on the right, present on the left. The right lower face drooped, with weak closure of the right eyelid, and there was a complete flaccid right hemiplegia. Tendon reflexes were diminished to absent in the right limbs, present and moderately active on the left. Abdominal and cremasteric reflexes were absent. The plantar reflex was absent on the right, flexor on the left. There was no response to painful stimuli on the right half of the body, whereas pinpricks on the left produced restless movements of the trunk and left extremities. Carotid pulsations were good bilaterally. Breath sounds were decreased over the right lower lobe. Heart sounds were inaudible. The abdomen was soft, with no palpable masses; peristaltic sounds were not heard.

The temperature was 99.2°F., the pulse 112 and the respirations 40. The blood pressure was 50 systolic; no diastolic pressure was obtainable.

A white-cell count was 5100. A hemoglobin was 16.0 gm. A lumbar puncture revealed fluid under an initial pressure equivalent to 120 mm. of water and a final pressure equivalent to 90 mm. of water, after withdrawal of 10 cc. of clear colorless fluid. The fluid contained 3 lymphocytes per cubic mm., and 41 mg. per 100 cc. of total protein. The colloidal gold curve was 0001333200.

The patient was given oxygen by mask and 0.8 mg. of Cedilanid intravenously. Peripheral pulsations became unobtainable and respirations increasingly shallow. About one hour before death, it was found that the right eye deviated upward and outward, whereas the left eye was in the midposition. Gurgling was heard on auscultation of the abdomen on one occasion. The patient died about six hours after admission.

Differential Diagnosis

Dr. Raymond D. Adams*: May I see the x-ray films?

Dr. James J. McCort: The first film was taken at the bedside on the first admission. Although not too satisfactory, it shows a large heart associated with pulmonary congestion. In a chest film taken ten months prior to the final admission, the lungs are seen to be relatively clear. There is enlargement of the heart in the region of both ventricles and patchy sclerosis of the aorta. The pulmonary vessels are not dilated. A gastrointestinal series made on the same date discloses widening of the mucosal folds and evidence of retained secretions in the stomach. The duodenal cap is markedly narrowed, deformed and constricted. Although a crater is not demonstrated the change described is the result of chronic duodenal ulceration.

Dr. Adams: What about the shadows in the right lobe of the lung that were mentioned?

Dr. McCort: In the initial examination that could be considered due to pulmonary congestion.

Dr. Adams: It was also reported on the second admission, wasn't it?

Dr. McCort: On the second examination the changes described are not striking and may represent a slight degree of scarring.

Dr. Adams: You feel that there is definite disease of the duodenum?

Dr. McCort: Very likely a chronic duodenal ulcer with scarring and contracture.

Dr. Adams: The way I would put all these findings together is somewhat as follows: I assume that the first illness was caused by coronary thrombosis and myocardial infarction. That would explain the chest pain radiating to the left arm, the pallor, the sweating and the neutrophilic leukocytosis. The electrocardiogram is also consistent with myocardial infarction. This electrocardiogram pattern would suggest a lesion in either the anterior part of the heart or the anteroseptal region. The patient was

*Chief, Neurology Service, Massachusetts General Hospital.

given the usual treatment for coronary thrombosis and did rather well, his only residual symptoms being the angina pectoris from time to time.

The postprandial epigastric pain relieved by soda and benefited by bland diet certainly indicates peptic ulcer, evidently in the posterior wall of the duodenum. The epigastric tenderness and the questionable hematemesis were all in keeping with this diagnosis. Moreover, the patient had had ulcer symptoms before, and a recurrence of symptoms of course is not unexpected. The gastric retention that was demonstrated on that admission indicates some blockage of the duodenum. Since the obstruction was relieved by medical treatment, I would assume it was due largely to spasm.

The last illness is more complicated. The patient had the epigastric pain, vomiting, and circulatory collapse with pallor, sweating and cold limbs. Certainly by the time he arrived in the hospital he was in a state of circulatory collapse with a blood pressure of 50. Since he had these two diseases, coronary sclerosis with myocardial infarction and recurrent peptic ulcer, the problem of course was to decide whether he now suffered from a complication of one of them. Either one could cause gastric pain. The complications of ulcer, I believe, that would cause shock are massive hemorrhage, of which there was no evidence — he was vomiting but not raising blood — and perforation with peritonitis. The abdomen was soft and nontender and gurgling was heard on one occasion. I find it difficult from these meager data to make a very good case for this pain and circulatory collapse being on the basis of a perforated peptic ulcer and peritonitis. Instead I would favor a recurrence of coronary thrombosis, the pain of which may be in the epigastrium or may even be absent. Of course circulatory collapse is not infrequent in coronary occlusion. This diagnosis could have been established by an electrocardiogram, of which we have no report.

Next a group of neurologic symptoms appeared, the first of which was coma. Coma coming on in a person with a blood pressure of 50 systolic may be on the basis of circulatory collapse alone. In fact, whenever the systolic blood pressure falls much below 70, there is likely to be some impairment in the state of consciousness. Its abrupt onset however is also consistent either with a convulsion or a stroke. No convulsions were observed at the onset of coma, which should exclude this mechanism. When he recovered consciousness, his speech was disturbed, and this as well as the right hemiplegia noted later establishes the possibility of some type of vascular lesion of the brain. The neurologic findings at that time are all understandable in terms of vascular disease in the left cerebral hemisphere. The diminished tendon reflexes on the paralyzed side were due to so-called spinal shock from a massive cerebral lesion. The turning of the head and eyes to the right is a bit odd, however, because with a destructive lesion in the left cerebral hemisphere the head and eyes ought to turn to the left. During a seizure, from a focus in the left cerebral hemisphere they would have turned to the right, but no convulsive movements were noted. I cannot explain this inconsistency.

There were diminished breath sounds over the right lower lobe. A number of neurologists have pointed out that an acute hemiplegia may cause some diminution in the expansion of the thorax. One may even be misled in some cases to assume the existence of a lung lesion from this finding. This diminution of expansion usually lasts only a few days, but as spasticity develops, it may recur.

The pupils were small, a finding I would attribute to the analgesic medicines that he was given. A hemianesthesia could be demonstrated by pinprick. This latter test also demonstrated that the coma was light because the pricking on the left side of the body caused restless movement of the left arm and leg.

From the neurologic findings I would postulate a lesion in the central part of the left hemisphere. It must have been quite extensive, since it involved the speech areas and motor and sensory parts of the brain. The rather light coma and the clear spinal fluid are much more in favor of the lesion being infarct necrosis than hemorrhage. I would suppose an occlusion had occurred in the terminal part of the left internal carotid artery or in the middle cerebral artery. Whether the deviation of the right eye upward and outward at the very end was merely an agonal finding or whether it represented a secondary brain-stem hemorrhage from a massive cerebral lesion I am not prepared to say; I would concede that latter possibility.

I have turned over in my mind the possibility of dissecting aneurysm of the arch of the aorta with obstruction of the internal carotid artery but rejected it because of the lack of certain symptoms and particularly because the left common carotid artery was felt to pulsate.

Under the circumstances presenting in this case the infarct could be caused by either an embolus from the heart or the thrombosis of an atherosclerotic artery during a period of circulatory collapse. I favor the diagnosis of generalized atherosclerosis and coronary thrombosis, old and recent, with myocardial infarction and a softening in the brain resulting from embolism. The occlusion was probably in either the terminal portion of the left internal carotid or the first part of the left middle cerebral artery. I would expect fairly extensive infarction in the left frontotemporal parietal region and possibly in the internal capsule and the lenticular nucleus on that side. The third diagnosis is duodenal ulcer, probably inactive with still some deformity.

In this case, I think one can be reasonably sure of the existence of a vascular lesion of the brain

because of the abrupt onset of the motor and sensory paralysis. One is required only to distinguish among brain infarction, brain hemorrhage and ruptured aneurysm. It may be worth while to consider some of the clinical differences among these conditions.

In brain infarction the onset of neurologic symptoms is sudden. The type of neurologic symptoms depends on the size and location of the lesion. Some degree of paralysis of one side of the body, hemianesthesia, homonymous hemianopsia and aphasia are the most common symptoms. Often in cases of brain infarction the patient does not lose consciousness or is in a state of semicoma, stupor or drowsiness. The cerebrospinal fluid with brain infarction is invariably clear even when the infarct is hemorrhagic and the pressure is normal. The patient usually improves to some degree, sometimes rapidly, and may live for quite a long period without further trouble, although, as everyone knows, there is always liability to recurrence.

Thrombosis may in many cases be distinguished from embolism as a cause of a softening. Thrombosis tends to cause a less abrupt onset of symptoms, often over a period of hours or a day or two. Or there may be two or three step-like progressions over a period of days or weeks. Embolism on the other hand is remarkable in its abruptness. Otherwise it is necessary to rely on collateral data to distinguish between thrombosis and embolism. Thrombosis occurs as a consequence of disease of the brain arteries, usually atherosclerosis. The majority of emboli arise in the heart, and nearly always there is some evidence of heart disease — often coronary arteriosclerosis, auricular fibrillation or bacterial endocarditis. Sometimes the pathologist cannot determine the source of the embolus. In our pathological material embolism is about as common as thrombosis, and the two together make up about 80 per cent of all cases of apoplexy. It has been possible to find the occlusion in 80 to 90 per cent of these cases by taking special precautions in examining the blood vessels in the neck and in the cranial cavity.

Brain hemorrhage differs from infarction. The patients nearly always have high blood pressures, though all patients with high blood pressure who suffer an apoplexy do not have hemorrhages. Again the onset is abrupt; the patients either lose consciousness immediately or may cry out with headache and face pain or dizziness and within a few hours lapse into a comatose state. The coma is almost invariably deep and appears to increase while the patient is under observation. It is possible however to determine the existence of hemiplegia by the slack face, arm and leg. The cheek on the paralyzed side puffs out with each expiration. Breathing is likely to be stertorous. The cerebrospinal fluid is under increased pressure and bloody in the majority of cases. Over 90 per cent of patients with brain hemorrhage die. Thus hemorrhage is distinguished from infarct on the basis of the severity of the coma, the rapidly progressive clinical course and the hemorrhagic cerebrospinal fluid.

In hemorrhage from ruptured saccular aneurysm, there may also be some degree of mental confusion or drowsiness, but coma is rare. The usual symptoms are headache, stiff neck and vomiting and these are of abrupt onset. Often there are no lateralizing neurologic signs, unless the hemorrhage has implicated the oculomotor nerve, optic nerve or chiasm or has extended into the brain, forming a meningo-cerebral hemorrhage. Even in cases of meningo-cerebral hemorrhage coma may not occur. In other words, the patient with hemiplegia and bloody cerebrospinal fluid who is conscious or only stuporous is likely to have an aneurysm as a cause of his hemorrhage, regardless of his age.

Of these more common types of apoplexy I believe the patient under discussion had an infarction of the brain due to occlusion of the left middle cerebral artery and, though unable to distinguish embolism from thrombosis with certainty, I favor the former.

Dr. Lawrence Barrows: I would like to ask how often one finds circulatory collapse in thrombosis or embolism?

Dr. Adams: I believe that is extremely rare. Shock, meaning circulatory collapse, is rare with any type of intracranial disease. In general, the blood pressure holds up remarkably well and it is the respiratory mechanisms that fail with brain disease. Whenever a patient with a brain lesion is seen with lasting circulatory collapse one looks for an explanation in extracranial organs.

Dr. Albert Damon: We were of the same opinion as Dr. Adams until we made the electrocardiogram, which showed no recent infarcts, but we were still unable to make any other diagnosis at that time.

Clinical Diagnoses

Cerebrovascular accident.
Arteriosclerotic heart disease.
Myocardial infarction, old.
Duodenal ulcer, inactive.

Dr. Adams' Diagnoses

Embolism in either the left internal carotid or middle cerebral artery.
Infarction of left frontotemporoparietal region and ?internal capsule and lenticular nucleus.
Generalized arteriosclerosis.
Myocardial thrombosis, old and recent.
Duodenal ulcer.

Anatomical Diagnoses

Perforation of duodenal ulcer.
Peritonitis, generalized.
Thrombosis, middle cerebral artery, left, recent.
Cerebral infarction, left hemisphere.
Coronary heart disease with old infarction, left ventricle.

Pathological Discussion

Dr. Austin L. Vickery: At autopsy when the abdomen was opened, 650 cc. of cloudy dirty fluid was encountered in which were floating some flecks of fibrin; the peritoneal surfaces were diffusely inflamed. The first portion of the duodenum was very thickened, fibrotic and adherent to the gall bladder and to the head of the pancreas. At a point about 3 mm. distal to the pyloric ring an aperture was present in the anterior wall of the duodenum about 5 mm. in diameter, which had free continuity with the peritoneal space. Pressure upon the stomach was productive of a free flow of gastric contents into the peritoneal cavity. This was an old peptic ulcer with considerable scarring, which had recently perforated, much to our surprise.

The heart, in brief, was enlarged, weighing 480 gm. There was an old area of massive infarction in the anterior wall of the left ventricle that also involved the anterior third of the interventricular septum. It was consistent with the episode about a year and a half previously. I think that the bulging of the thin ventricular wall, at the site of the old infarction, may have accounted for some of the enlargement of the heart in the last x-ray films.

Dr. Richardson will discuss the findings in the brain.

Dr. Edward P. Richardson, Jr.: At the time of post-mortem examination the internal carotid and vertebral arteries in the neck were both injected with water and were found to be patent. In the left middle cerebral artery where it enters the Sylvian fissure there was a dark-red thrombus occluding and distending the artery. This was in a portion of the artery immediately distal to the first large branch given off to the superior surface of the temporal lobe. At that bifurcation there was an atherosclerotic plaque; the thrombus filled the main trunk of the artery from this point on. On section of the brain, pallor of the cerebral cortex was noted in the frontal, cerebral, and parietal portions of the left cerebral hemisphere, in the territory of supply of the left middle cerebral artery. The left temporal lobe and basal ganglia appeared normal, as did the entire right hemisphere.

On microscopical examination the middle cerebral artery was found to be occluded by very recent thrombus, which was not adherent to the walls of the vessel. Sections of the cerebral cortex showed acute, recent degenerative changes in the nerve cells in the microscopically pale areas, contrasting with the generally normal appearance of the neurons elsewhere.

The findings indicate recent thrombosis of the left middle cerebral artery, and recent infarction of the corresponding portion of the left cerebral hemisphere. The thrombus might have been embolic, but its location in an atheromatous part of the vessel suggests that it originated there. The remainder of the brain was unremarkable.

Dr. Vickery: We searched very carefully in the heart for any evidence of mural thrombi and found none. There was no evidence of recent infarction either.

Dr. Adams: That could have been formed at the time when the blood pressure was at the shock level.

Dr. Vickery: Yes. In retrospect, it appears that the case represented an initial intra-abdominal catastrophe, the characteristic symptoms of which were largely masked by a subsequent hemiplegia that was probably brought about by the state of circulatory collapse induced by generalized peritonitis.

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THE GROWTH OF A SPECIALTY

PHILOSOPHY has been defined as that body of principles or of moral wisdom from which the more detailed branches of learning are separated, as icebergs are dropped from the mature end of a glacier; Denny-Brown, in his Shattuck Lecture, published elsewhere in this issue of the *Journal*, has presented a similar concept of the philosophy pertaining to medical progress, applying it to his own field of neurology.

As with the specialties in general, neurology first came into existence because of certain manifestations of aberrant nature that could be identified with a single body system. Before long, however, it seemed as if this budding science might wither and be lost, as general paresis, tabes dorsalis and combined system disease tended to disappear from the list of ills with which man has been visited. Its salvation has resulted from the widening of its field, as it has become linked more securely with general medicine, despite its continuing tendency also to become restricted to smaller component parts as isolated investigations went deeper.

Neurology, in its full flowering, can no more be limited to the nervous system than dermatology can be considered as only skin deep or even as a merely two-dimensional study, like painting, in which depth is an illusion of perspective. With all the separation into finely drawn entities that is bound to occur, and with the trend toward gun-barrel visualization of isolated and restricted areas, the realization always comes, to those who have retained their awareness, that the beads have to be rethreaded to recreate a pattern and that the various divisions of medicine must eventually be resynthesized into a comprehensive whole.

On the relation to internal medicine of any such special study and service as neurology, its strength and even its continued survival depend; the fruit cannot develop away from the vine; the stethoscope is as essential a tool to the neurologist as is the reflex hammer or the tuning fork. Technics, indeed, are hazardous if considered outside their relation to the whole. The radiologist, the anesthesiologist or the bronchoscopist knows that he must be first the physician and then the technologist; the ophthalmologist must be something more than an ophthalmoscopist. "The neurologist," as Denny-Brown points out so clearly, "must first be an internist. His inspiration is in the general medical wards; his technics are those of internal medicine."

So, with the realization that much that occupies the neurologist is simply (or far from simply) the neurologic manifestations of systemic disorder, it becomes increasingly obvious that the broader the base on which he stands, the more effective he is in his specialty. "Neurologic medicine is greater than the sum of the contributions of neurologists, and its problems invite the continued attention of all branches of internal medicine."

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The same can be said, in greater or lesser degree, of all the specialties. Only when they are reintegrated into the great body of organized medical knowledge do they reach their real fulfillment.

NURSING REORGANIZES

NURSING is realigning itself into two national organizations for the purpose of working more effectively toward a common goal: namely, better nursing care for the people of the United States. The need to co-ordinate national effort in nursing has been repeatedly demonstrated during the past twenty-five years — but never more acutely than during World War II, when the ever-mounting demand for nursing service made it imperative that a more closely-knit organizational structure be developed.

In 1944, the boards of directors of the American Nurses Association, the National League of Nursing Education and the National Organization of Public Health Nursing accordingly voted to undertake a joint survey of their organizational structure, administration, function and facilities to determine whether a better means could be found through which they might work most advantageously toward the improvement of nursing services and education. In 1945, the Association of Collegiate Schools of Nursing, the National Association of Colored Graduate Nurses and the American Association of Industrial Nurses joined in the reorganization study.

The search for a structure that would provide greater unity for nursing organizations and their programs has been a democratic process throughout. The individual nurse has been asked to help in reaching all decisions. Several plans were proposed and workshops were held throughout the country. A major question to be answered before any real progress could be made was: "Does nursing need one or two organizations, or should it remain in *statu quo*?" Gradually, the national opinion of members crystallized in favor of a two-organization structure, and in 1950 the six participating national organizations voted to realign into a revised American Nurses Association and the National League for Nursing — a new organization.

The American Nurses Association will be a continuing organization with a number of changes in its present structure, especially concerning sections and the House of Delegates. There will be more national sections and greater section activity than in the past. The revised plan for the American Nurses Association provides sections for groups determined according to the following occupations: private duty, general duty, public health, institutional nursing-service administration, educational administration, consultation and teaching, industrial nursing and an unaffiliated or special-groups section. Each section will define the function, standards and qualifications for practice within its own field. Likewise, each section will plan its own program and budget. Sections in the state nurses' associations will be strengthened by having proportional representation in the American Nurses Association House of Delegates.

The American Nurses Association will promote the professional, general and economic welfare of professional nurses and help them to become the best possible practitioners as individuals and as members of a profession; students of professional nursing schools will be members through their affiliated student-council organization.

The National League for Nursing, the proposed name for the new organization, will foster the development and inprovement of organized nursing services and education for nursing, so that the nursing needs of the people will be filled. The National League for Nursing will be unique among membership organizations in the United States — and, so far as is known, in the world. There will be two types of membership; individual and community agency. Through the National League for Nursing it will be possible for nurses in all occupational fields and positions in nursing, members of boards and committees associated with nursing services and educational units, members of allied professional groups and other citizens to co-ordinate their efforts toward the improvement of the quality and quantity of nursing services in communities.

The new organization will have two membership divisions — a Division of Nursing Services and a Division of Nursing Education. The Division of Nursing Education will foster the development and improvement of education for nursing. The Division of Nursing Services will further the development

and general betterment of nursing services. In brief, the National League for Nursing will be a "community-centered" organization in which the points of view of nurses and other citizens, both as individuals and as representatives of the community health and educational agencies, will be pooled to effect co-ordinated action in nursing for the common good.

In the National League for Nursing, students of professional nursing will also be participating members through their accredited schools of nursing.

In order that the National League for Nursing may achieve its objective, it is important that a plan be developed for the improvement of practical, as well as professional, nursing service and education. A special committee will guide the National League for Nursing program as it relates to practical nursing, with the aim of developing a departi ent for schools of practical nursing in the Γ `sion of Nursing Education.

Details for realigning into two national organizations have been worked out by authorized national committees and will be acted on in the summer of 1952. Thus, nursing will have a new national organizational structure before next fall.

NEW ENGLAND'S HEALTH

JUNE, the month of roses and of brides, is also a close runner-up to May as a choice time for medical meetings, to the point where it has apparently become necessary for Connecticut and Massachusetts to run a two-ring circus on June 18, 19 and 20.

On these final days of spring the sixth annual Massachusetts Public Health Conference, sponsored by the Massachusetts Public Health Association, the Massachusetts Department of Public Health and the University of Massachusetts, will take place on the campus of the University of Massachusetts at Amherst. In addition to four general sessions, the Public Health Association, the Massachusetts Central Health Council, the Massachusetts Water Works Association, the United Cerebral Palsy Association of Massachusetts and the Massachusetts Section of the National Association of Sanitarians will hold their own meetings during the period of the Conference.

A number of vital topics will be discussed, including civil defense, the union health program and fluoridation of water supplies. Moving pictures will be shown with such titles as "So Much for So Little," portraying the services of local health departments; "Circulation" and "Heart to Heart," suggesting an anastomosis but not confirming it; "Cheers for Chubby," presenting in cheery fashion the conflict with the calories, and "The Traitor Within," which "tells about cancer in the inimitable Walt Disney style." In line with these graphic methods of impressing the public, or perhaps as a more majestic flashback to the days of Dante, the subject to be presented at the annual dinner of the Massachusetts Public Health Association will be "The Comedy of Health."

Concurrently at Storrs, Connecticut, under the sponsorship of the six New England state departments of health, the United States Children's Bureau and the Public Health Service, the New England Health Association, the Harvard School of Public Health and Simmons College, and with most of the health organizations of Connecticut participating, the eighteenth New England Health Institute will be held at the University of Connecticut.

At this institute many of the same general problems will be presented that will be discussed at the Massachusetts conference. Even as success is wished to each of these important meetings of the minds, the suggestion may be in order that perhaps starting times should be arranged ahead, as on a public golf course.

UNION OF REPORTING SECRETARIES

THE British U.R.S.L.S. (Union of Reporting Secretaries to Learned Societies), according to a peripatetic correspondent of the London *Lancet*, is expected shortly to be called on to protest against the habit, increasingly common among lecturers at least in Merrie England, "of spreading their light in dark places." The speakers especially under fire by this particular peripatetic scribe are those who, after acknowledging their introduction and relating one humorous anecdote, have the lights switched off and spend their allotted time in the dark discussing slides, to the confusion of the utterly frustrated R.S.L.S. who is supposed to be taking notes.

At the opposite end of the peripatetic spectrum is the lecturer described in a previous issue of the *Lancet* who, having no slides to show and with no intention of showing them, in a perfect paroxysm of unintentional perversity finds the buzzer button on the lectern and grips it, leans on it or sits on it through the course of his remarks. These are not all the difficulties encountered by reporting secretaries to learned societies; they are only two of them.

When the legislature, or private charity, shall provide a receptacle for that degraded portion of society, drunkards, it will be a triumph of benevolence and the institution will doubtless be filled.

Boston M. & S. J., *June 2, 1852*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

FLYNN — George C. Flynn, M.D., of Indian Orchard, died on May 9. He was in his fifty-third year.

Dr. Flynn received his degree from Tufts College Medical School in 1924. He was a member of the Springfield Academy of Medicine and a fellow of the American Medical Association.

He is survived by his widow and two children.

LYNCH — William F. Lynch, M.D., of Worcester, died on May 2. He was in his seventy-fourth year.

Dr. Lynch received his degree from Harvard Medical School in 1908. He was a member of the New England Cancer Society, the American College of Surgeons and the American Board of Surgery, a former president of the Worcester District Medical Society and a fellow of the American Medical Association.

He is survived by his widow.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR APRIL, 1952

RÉSUMÉ

DISEASE	APRIL 1952	APRIL 1951	SEVEN-YEAR MEDIAN
Chancroid	2	9	2
Chicken pox	1826	1655	1751
Diphtheria	5	7	18
Dog bite	1354	1395	1216
Dysentery, bacillary	0	5	7
German measles	3434	266	258
Gonorrhea	125	130	254
Granuloma inguinale	0	0	0
Lymphogranuloma venereum	0	0	1
Malaria	3	1	3
Measles	8579	1995	2022
Meningitis, meningococcal	5	6	6
Meningitis, Pfeiffer-bacillus	5	3	3
Meningitis, pneumococcal	2	1	2
Meningitis, staphylococcal	0	0	0
Meningitis, streptococcal	1	0	0
Meningitis, undetermined	8	2	3
Mumps	1205	1608	1346
Poliomyelitis	2	0	0
Salmonellosis	5	0	6
Scarlet fever	474	578	652
Syphilis	136	93	256
Tuberculosis, pulmonary	250	222	225
Tuberculosis, other forms	24	18	12
Typhoid fever	3	1	2
Undulant fever	0	1	3
Whooping cough	121	171	476

COMMENT

Diseases below the seven-year median are diphtheria, scarlet fever and whooping cough. For all three of these diseases the number of cases reported in April represents the lowest ever for this month in our records.

Diseases markedly above the seven-year median are German measles and measles.

The number of cases of German measles reported is the highest for any month since June, 1943, the year with the greatest number in our records. The 3434 cases of German measles reported are well above the 2146 cases reported for the previous month and represent an incidence of more than twelve times that of April, 1951.

Measles, although still greatly above the seven-year median, is below the 12,000 cases reported in March, 1952, and is the lowest number of cases for this year. Of 36 cities and towns in Massachusetts with a population of over 25,000, 25 show a moderate to marked decrease in the number of measles cases reported in the previous month of March. Eleven cities show an increase: New Bedford, Lynn, Brockton, Waltham, Arlington, Newton, Fitchburg, Revere, Weymouth, Framingham and Boston.

GEOGRAPHICAL DISTRIBUTION OF CERTAIN DISEASES

The following diseases were reported from the communities named:

Diphtheria: Dalton, 1; Melrose, 1; New Bedford, 1; Revere, 1; Springfield, 1; total, 5.

Dysentery, amebic: Cambridge, 1; total, 1.

Encephalitis, infectious: Franklin, 3; Quincy, 1; Watertown, 1; Westport, 1; total, 6.

Hepatitis, infectious: Camp Edwards, 1; Fort Devens, 3; Otis Air Force Base, 1; Lowell, 1; Quincy, 1; Wellesley, 2; Worcester, 4; total, 13.

Malaria: Camp Edwards, 2; Fort Devens, 1; total, 3.

Meningitis, meningococcal: Cambridge, 1; Fall River, 1; Medford, 1; Newton, 1; Worcester, 1; total, 5.

Meningitis, Pfeiffer-bacillus: Ashby, 1; Hingham, 1; Hull, 1; Lynnfield, 1; Stoughton, 1; total, 5.

Meningitis, pneumococcal: Stoneham, 1; Worcester, 1; total, 2.

Meningitis, streptococcal: Berkley, 1; total, 1.

Meningitis, undetermined: Fall River, 1; Fort Devens, 1; Middleboro, 1; Milford, 1; Norwood, 1; Taunton, 1; Worcester, 2; total, 8.

Poliomyelitis: Dracut, 1; Randolph, 1; total, 2.

Salmonellosis: Cheshire, 2; Sheffield, 1; Springfield, 2; total, 5.

Septic sore throat: Boston, 4; Dedham, 1; Holland, 1; Mansfield, 1; Saugus, 10; Worcester, 1; total, 18.

Trichinosis: Adams, 3; Brockton, 1; Everett, 1; total, 5.

Typhoid fever: Gloucester, 1; Quincy, 2; total, 3.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS

The June schedule for Consultation Clinics for Crippled Children in Massachusetts follows:

ORTHOPEDIC CLINICS	DATE	CLINIC CONSULTANT
Salem	June 2	Paul W. Hugenberger
Gardner	June 3	Carter R. Rowe
Haverhill	June 4	William T. Green
Greenfield	June 5	Charles L. Sturdevant
Lowell	June 6	Albert H. Brewster
Lynn*	June 9	Daniel M. Killoran John J. Crowley
Brockton	June 12	George W. Van Gorder
Springfield	June 17	Garry deN. Hough, Jr.
Pittsfield	June 18	Edward J. Coughlin, Jr.
Fall River	June 23	David S. Grice
Hyannis	June 26	Paul L. Norton
Worcester	June 27	John W. O'Meara

RHEUMATIC-FEVER CLINICS	DATES
North Reading	June 3, 10, 17, 24
Fitchburg	June 4, 11, 18, 25

PLASTIC CLINICS	HELD	CONSULTANT
Eastern Massachusetts	Semi-monthly	Bradford Cannon
Western Massachusetts	Monthly	Joseph M. Baker

Physicians referring new patients to clinics should get in touch with the district health officer to make appointments. Patients are seen by appointment only.

*This clinic serves Lynn, Lynnfield, Saugus, Nahant, Revere, Chelsea, Everett, and Winthrop. Referrals should be made directly to the Lynn Hospital.

NONCLINICAL NOTES

Dr. Shields Warren, pathologist at New England Deaconess Hospital, Boston, has resigned as director of the biology-medicine division of the Atomic Energy Commission. Dr. Warren, head of the division since its establishment in 1947, has been termed "one of the architects of the atomic energy program." During the four and a half years in which this program has been in effect, there have been no radiation deaths at any of the national laboratories.

BOOK REVIEWS

Diseases of the Heart and Circulation. By Paul Wood, O.B.E., M.D. (Melbourne), F.R.C.P. (London). 8°, cloth, 589 pp., with illustrations. Philadelphia: J. B. Lippincott Company, 1951. $12.50.

This book is one more in the growing list of volumes covering the entire field of cardiovascular disease. It reflects the British belief that "there is already plenty of evidence to show that we are in danger of losing our clinical heritage and of pinning too much faith in figures thrown up by machines." Hence the attempt of the author "to maintain a proper balance between man and his instruments." It has been written primarily for graduates interested in clinical cardiology and well fulfills this purpose.

The approach is physiologic and etiologic rather than anatomic. The sections on radiographic diagnosis and electrocardiography are excellent, and the quality of the paper permits good reproductions of x-ray films. The method of mounting electrocardiograms is highly practical and might well be recommended as standard procedure for the 12-lead technic, as it places the tracings in logical positions relative to the Einthoven triangle.

Phonocardiography receives only 15 lines of discussion, with little regard to the advances of the past ten years.

Congestive failure is covered in 35 pages. The dietary recommendations naturally have a British flavor, as in the advice to avoid Bovril and winkles in a low-sodium diet and to eat, as the best "offal," sweetbreads, fresh tongue and liver.

Acupuncture of the legs is advised as a late resort in the relief of edema but without mention of the routine use of penicillin to prevent infection.

Congenital heart disease is given a clinically adequate description, as are rheumatic fever and carditis and the other major etiologic types of heart disease. Nonspecific, benign or idiopathic pericarditis, which is relatively common in this country, is considered in a short paragraph. Its possible viral origin is not mentioned, and the use of penicillin or streptomycin, rather than aureomycin, is recommended. It is interesting that the words "virus" and "viral" do not appear in the index of this book.

In the treatment of cardiac infarction three to six weeks' bed rest is advised. Conservatism in the use of digitalis is stressed, on the basis of a paper published in 1938.

The useful protein-bound-iodine test of thyroid function is not mentioned in the chapter on thyrotoxicosis.

It is surprising to find Duroziez's name consistently misspelled.

As is true of all textbooks covering rapidly expanding fields, this one of necessity cannot be used to answer the latest questions of diagnosis and therapy, but it is a sound, well presented reference work that will be useful on many medical bookshelves.

HOWARD B. SPRAGUE, M.D.

The Conquest of Malaria. By Jaime Jaramillo-Arango, M.D. 8°, cloth, 125 pp., with 36 plates and frontispiece. London: William Heinemann Medical Books, Ltd., 1950. 21s net.

This authoritative monograph, a new and provocative account of the age-old problem of malaria and its cure, comes from the former head of the medical school at Bogotá and recent Colombian Ambassador to Great Britain. Taking advantage of the wealth of source material for medico-historical research in the British capital, the author has completed a twenty-year study of the disease that was begun in South America, extended into Spanish libraries and the Vatican treasure house and finally polished in its English version by the deputy librarian of the Wellcome Historical Medical Library in London. It is admirable in every way.

The mosquito-malaria theory and the progress achieved in the prevention and treatment of malaria form two large sections of the book, the latter culminating in an account of the discovery of Paludrine in 1944. Each step in the development is considered in relation to previous investigations, and adequate documentation accompanies the text. There is an abundance of illustrations.

The middle section of the book consists in a critical review of the basic facts in the history of cinchona. Here the author is most helpful; his conclusions, based on widespread evaluations, are convincing, although often differing from generally accepted views. He believes that malaria was known to the Indians in pre-Columbian America and that cinchona was familiar to them also. The legend of the cure of the Countess of Chinchon by the bark about 1630–1640 is abandoned, although with reluctance because of its charm and picturesqueness. It is too conjectural to stand up under close historical scrutiny. The drug was introduced into Europe between 1630 and 1635. Thomas Bartholin reproduced the earliest known picture of the cinchona tree in a book published in 1661.

Further chapters are concerned with the error of Linnaeus in writing the Countess's name, the etymology of the word "quinaquina," the early controversy about the medicinal value of cinchona and notes on its botanical classification. The appendix gives reference to all texts, with frequent citations of pertinent passages in the original language. Footnotes at the bottom of each page make for ready reference. Much information unknown to previous writers has been unearthed by the author and every statement is traced to its source. The index is adequate.

HENRY R. VIETS, M.D.

KANSAS STATE COLLEGE OF AGRIC. & SCIENCE LIBRARY JUN 10 1952 MANHATTAN KANSAS

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Manual of Tumor Nomenclature and Coding. Prepared by Subcommittee of the Statistics Committee, American Cancer Society. 4°, cloth, 119 pp. New York: American Cancer Society, Incorporated, 1951. $2.50.

The American Cancer Society has now established a standard code for the histogenetic classification of neoplasms and a malignancy code. The various types of tumors, proceeding from the general to the special, are arranged numerically. A comprehensive index is appended to the text. The volume is well published and should be in all medical libraries.

Internal Medicine: Its theory and practice. Fifth edition. Edited by Michael G. Wohl, M.D., associate professor of medicine, Temple University School of Medicine, chief of nutrition clinic, Philadelphia General Hospital, and chief of endocrine clinic, Temple University Hospital. With eighty contributors. Originally edited by John H. Musser, M.D. 4°, cloth, 1563 pp., with 236 illustrations and 10 plates in color. Philadelphia: Lea and Febiger, 1951. $15.00.

The fourth edition of this standard work on internal medicine was published in 1944. This new edition has been thoroughly revised to bring the material up to date. The book is designed primarily for the medical student and the physician engaged in general practice. Lists of selected references are included under the various subjects, and there is a comprehensive index. The book is well published and should be in all medical libraries.

Wissenschaftstheoretische Aufsätze für Ärzte. By Prof. Dr. G. Ricker. Foreword by Dr. V. Schaefer. Second edition. 8°, paper, 82 pp. Stuttgart: Georg Thieme, 1951. DM 5.70. Distributed by Grune and Stratton, Incorporated, New York.

This is a reissue of Professor Ricker's philosophical discussion of man, his body and his mind, first published in 1936.

Die Trübungsformen der menschlichen Linse. By Dr. Hans Sautter, apl. Professor und Oberarzt an der Universitäts-Augenklinik Tübingen. 8°, cloth, 139 pp., with 191 illustrations. Stuttgart: Georg Thieme, 1951. DM 49.80. Distributed by Grune and Stratton, Incorporated, New York.

This monograph is devoted to a discussion of the aciniform appearances occurring in the lens of the human eye. Special emphasis is placed on cataracts of various kinds and also on cloudiness of the lens in general diseases and poisoning. The type, printing and illustrations are excellent. There is a bibliography of 14 pages and a good index. The monograph should be in all collections on ophthalmology.

Experiment in Dental Care: Results of New Zealand's use of school dental nurses. By John T. Fulton, D.D.S., dental services adviser, Children's Bureau, Social Security Administration, Federal Security Agency, Washington, D. C. 8°, paper, 87 pp., with 12 illustrations and 10 tables. Geneva: World Health Organization, Palais des Nations, 1951. 5/–, $1.00, Sw. fr. 4.– (World Health Organization Monograph Series No. 4.)

In this report Dr. Fulton surveys New Zealand's dental program, which is operated by the Public Health Department. This program has been a controversial subject the world over, because it entrusts a large part of the dental care of children to young women, who operate school dental clinics after two years' training. This training is discussed in the report. The dental profession in the country is surveyed and the final chapter is devoted to the history of the development of the national dental service.

Leibesübungen mit Körperbeschädigten: Ein Lehr- und Arbeitsbuch für Körperbehinderte und ihre Betreuer. By Hans Lorenzen, Oberstudienrat, Köln. 8°, cloth, 218 pp., with 182 illustrations. Stuttgart: Georg Thieme, 1951. DM 7.50. Distributed by Grune and Stratton, Incorporated, New York. (Arbeit und Gesundheit, New Series No. 45.)

This monograph is devoted to the subject of exercise and gymnastics as remedial measures for traumatic conditions. The text is divided into three main parts: organization of a program; general gymnastics, medicine ball and tumbling; swimming, diving and lifesaving. The publishing is excellent and the illustrations informative. It should prove useful to persons interested in physical training and remedial exercises.

Statistics for Medical Students and Investigators in the Clinical and Biological Sciences. By Frederick J. Moore, M.D., associate professor of experimental medicine, University of Southern California School of Medicine, Frank B. Cramer, B.A., research fellow, and Robert G. Knowles, M.S., research associate, Department of Experimental Medicine, University of Southern California School of Medicine. 8°, cloth, 113 pp., with 11 illustrations and 16 tables. Philadelphia: The Blakiston Company, 1951. $3.25.

This manual is devised for persons interested in understanding complicated statistical tables. It considers variation in the normal curve of error, fitting the normal curve of error to the data, sampling distributions and tests of significance, the problem of non-normal distribution and the general aspects of the design of experiments and presentation of results.

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711 Medical Maxims. By William S. Reveno, M.D., assistant professor of clinical medicine, Wayne University Medical College, attending physician, Harper Hospital, and consulting physician, Detroit Receiving and Highland Park General Hospitals, Detroit, Michigan. With forewords by Frederick A. Coller, M.D., and William J. Kerr, M.D. 16°, cloth, 197 pp. Springfield, Illinois: Charles C Thomas, 1951. $3.75.

Dr. Reveno has created a new type of book on medical maxims. The 711 items have been selected with the idea that they would have ready application in everyday practice. The text is divided into nine sections, arranged according to various classes of diseases. A comprehensive index of 75 pages lists the various diseases mentioned in the text proper.

NOTICES

SOUTH END MEDICAL CLUB

The South End Medical Club will celebrate its twenty-fifth anniversary at the Prendergast Preventorium of the Boston Tuberculosis Association, 1000 Harvard Street, Mattapan, on June 24. All physicians who have addressed the club in past years will be invited to participate.

At noon, Dr. Maxwell Finland, associate professor of medicine at Harvard Medical School, will speak on "The Chemotherapy of Tuberculosis." Luncheon will be served at 1:00 p.m.

SOCIETY MEETINGS AND CONFERENCES

MAY 29–31. American Academy of Dental Medicine. Page 476, issue of March 20.

JUNE 3–28. Springfield Hospital. Page 838, issue of May 22.

JUNE 5. Boston City Hospital House Officers' Association. Page 760, issue of May 8.

JUNE 5. New York Society for Circulatory Diseases. Page 676, issue of April 4.

JUNE 5–8. American College of Chest Physicians. Page 280, issue of February 14.

JUNE 6 AND 7. American College of Cardiology. Page 760, issue of May 8.

JUNE 6–8. International Academy of Proctology. Page 800, issue of May 15.

JUNE 7 AND 8. Society for Investigative Dermatology, Inc. Page 676, issue of April 24.

JUNE 9 AND 16. New England Hospital. Applied Basic Science Lectures. Page 838, issue of May 22.

JUNE 18–20. Massachusetts Public Health Conference. Amherst. Page 879.

JUNE 18–20. New England Health Institute. Page 760, issue of May 8, and page 879 of this issue.

JUNE 19–21. American Association of Genito-Urinary Surgeons. Page 34, issue of March 13.

JUNE 22–26. American Society of Medical Technologists. Twentieth Annual Convention. Portland, Oregon.

JUNE 23–25. Military-Civilian Medical Symposium. Murphy Army Hospital, Waltham.

JUNE 24. South End Medical Club. Notice above.

JULY 7–11. International Congress of Dietetics. Page 434, issue of March 13.

JULY 7–12. International Diabetes Federation. Page 316, issue of February 21.

JULY 8–11. Thirteenth British Congress of Obstetrics and Gynecology. Page 916, issue of December 6.

JULY 8–14. Commonwealth and Empire Health and Tuberculosis Conference. Page 792, issue of November 15.

JULY 14–18. Tuberculosis Symposium. Page 800, issue of May 15.

JULY 14–19. International Congress of Physical Medicine. Page 998, issue of June 28.

JULY 24–26. Conference on Aging. Page 559, issue of April 3.

AUGUST 25–29. American Congress of Physical Medicine. Page 476, issue of March 20.

AUGUST 31–SEPTEMBER 6. Interamerican Congress of Cardiology. Page 422, issue of March 27.

SEPTEMBER 7–9. Combined session of the New Hampshire and Vermont State Medical Societies. Mount Washington Hotel, Bretton Woods, New Hampshire.

OCTOBER 28–30. New England Postgraduate Assembly. Hotel Statler, Boston.

OCTOBER 29. New England Obstetrical and Gynecological Society. Annual Meeting. Hotel Somerset, Boston.

NOVEMBER 2–7 AND 10–21. Courses in Laboratory Diagnosis of Tuberculosis. Page 354, issue of February 28.

JULY, 1953. International Congress on Medical Librarianship. Page 316, issue of February 21.

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, JUNE 5

THURSDAY, JUNE 5

8:30–10:00 a.m. Fracture Conference. Boston City Hospital.

*9:00–10:00 a.m. Grand Rounds. Robert Breck Brigham Hospital.

9:00 a.m. Cardiac Rounds. House of the Good Samaritan.

*9:00–10:00 a.m. Cardiac Grand Rounds. Main Amphitheatre, Children's Medical Center.

9:30 a.m. Eye-Nerve Conference. Ether Dome, Massachusetts General Hospital.

12:00 m.–1:00 p.m. Weekly guest speaker. Stearns Auditorium, New England Center Hospital.

*4:00–5:00 p.m. Medical Division Lecture. Mount Auburn Hospital, Cambridge.

*7:00 p.m. Boston City Hospital House Officers' Association. Cheever Amphitheatre, Dowling Building, Boston City Hospital.

*7:30 p.m. Anesthesiology Conference. Lahey Clinic.

(Notices concluded on page xi)